Cost-Effectiveness of Adding Bed Net Distribution for Malaria Prevention to Antenatal Services in Kinshasa, Democratic Republic of the Congo

Sylvia I. Becker-Dreps,* Andrea K. Biddle, Audrey Pettifor, Gertrude Musuamba, David Nku Imbie, Steven Meshnick, and Frieda Behets

Abstract. We evaluated the cost-effectiveness of distributing insecticide-treated bed nets (ITNs) for malaria prevention at antenatal clinics in Kinshasa, Democratic Republic of the Congo. A decision tree model was used to estimate costs, outcomes, and incremental cost-effectiveness for 17,893 pregnant women attending 28 antenatal clinics who received long-lasting ITNs free of charge. Costs including purchase, transportation, storage, and distribution of ITNs were derived from program records. The ITN efficacy and other parameters were derived from peer-reviewed literature. Outcomes modeled included low birth weight (LBW) deliveries, infant deaths averted, life-years saved (LYs), and disability-adjusted life-years (DALYs) averted. Deterministic and probabilistic sensitivity analyses were conducted. For the 17,893 women in our program, ITN distribution would be expected to avert 587 LBW deliveries and 414 infant deaths. The incremental cost-effectiveness was US $17.22 per DALY averted (95% confidence interval [CI] = US $8.54–$30.90), US $15.70 per LY saved (95% CI = US $7.65–$27.68), and US $411.13 per infant death averted (95% CI = US $353.95–$1,085.89). If resources were constrained, the greatest benefit would be among women in their first through fourth pregnancies. Thus, ITN distribution is a cost-effective addition to antenatal services.

INTRODUCTION

Use of insecticide-treated bed nets (ITNs) can effectively prevent malaria. Their use by pregnant women reduces the incidence of low birth weight (LBW) by 23% in women through fourth pregnancies, and use by children reduces all-cause mortality by 17%.1,2 The protective effect observed in children is strongest during the first year of life.3 Because infants in sub-Saharan Africa typically sleep with their mothers, distribution of ITNs at the antenatal clinic benefits pregnant mothers and subsequently their infants.

The World Health Organization recommends that pregnant women and children less than five years of age in sub-Saharan Africa should have the highest priority for receiving ITNs.4 However, possession of ITNs in sub-Saharan Africa remains low, with only 6.7% of households owning one.5 The antenatal clinic is a logical target for ITN distribution because 70% of women in sub-Saharan Africa will visit the antenatal clinic during their pregnancies.6 Also, integrating programs and using existing infrastructure can contain costs, an important objective in resource-poor countries that must choose between many needed interventions.

In this context, we estimated the programmatic costs, benefits, and the cost-effectiveness of adding ITN distribution at antenatal clinics from the health provider perspective. During November 2005–September 2006, we assisted 28 antenatal clinics in Kinshasa, Democratic Republic of the Congo (DRC), with the implementation of a prevention of maternal-to-child transmission (PMTCT) of human immunodeficiency virus (HIV) program. As part of these PMTCT activities, 17,893 women were given long-lasting ITNs free of charge. Malaria is common among pregnant women in Kinshasa; 60% of women at a Kinshasa maternity hospital had a positive malaria smear during pregnancy at the time our intervention was conducted.7

We determined the cost-effectiveness of adding ITN distribution using the actual costs of this intervention derived from program records. Using a decision model, we modeled the estimated infant deaths and LBW deliveries averted by ITN use, using data from published studies of ITN efficacy.1,2

MATERIALS AND METHODS

Program site. Distribution of ITNs was conducted at 28 antenatal clinics providing PMTCT services in Kinshasa. These antenatal clinics are managed by the DRC Ministry of Health or by non-governmental organizations, mainly religious organizations. A total of 26–320 new antenatal patients attended the clinics per month, which resulted in a total of 33,541 patients during the course of the intervention. Prior to the intervention, none of the clinics distributed bed nets. In addition to PMTCT services with single-dose nevirapine, the clinics provide a minimum antenatal package including malaria diagnosis and treatment, intermittent preventive treatment of malaria in pregnancy (IPTp), iron and folate supplementation, nutrition counseling, syphilis diagnosis and treatment, tuberculosis diagnosis and treatment, tetanus immunizations, and family planning counseling.

Intervention. We distributed 17,893 long-lasting ITNs free of charge to pregnant women attending antenatal clinics providing PMTCT services in Kinshasa. During November 2005–September 2006, the implementation of the program occurred in a step-wise manner as clinic staff received training and the ITNs became available for distribution. Two nurses per site received five days of comprehensive malaria education prior to distribution. Nurses then distributed ITNs during antenatal educational sessions, providing information on correct ITN use and malaria transmission. Of 33,541 women who received antenatal care during this period, only 17,893 women received ITNs because the program was phased in as sites received training and ITNs for distribution. Also, a change in the funding...
arrangements made the ITNs unavailable for a short time at all sites. Finally, ITNs were not distributed if both trained nurses at a site were absent from work. Women who missed distribution at their first visit may have received an ITN at a subsequent visit if trained staff and ITNs were available. However, if women did not return for additional visits, they did not receive an ITN.

We used long-lasting insecticide-treated nets (Permanet® 2.0; Vestergaard-Frandsen, Lausanne, Switzerland) donated by the Global Fund and the U.S. Centers for Disease Control and Prevention. Long-lasting ITNs maintain efficacy without insecticide re-treatment for up to 20 washes. Because bed nets are generally washed infrequently, these long-lasting ITNs would maintain efficacy when used during pregnancy and one year postpartum.

Ethical clearance. This study was reviewed and approved by the Biomedical Institutional Review Board of the Office of Human Research Ethics at the University of North Carolina at Chapel Hill.

Description of model and parameters. Using a decision tree model, we estimated the number of LBW deliveries and infant deaths averted, life-years (LYs) saved, and disability-adjusted life-years (DALYs) averted for the cohort who received ITNs to use during their pregnancies and for their infants after birth. The model takes the health care provider perspective and uses a time horizon that runs from the receipt of the ITNs to one year postpartum. We then simulated disability-adjusted life expectancy for the infants. Model parameters and corresponding data sources are summarized in Table 19–24 and are described below.

We modeled the outcomes for the entire cohort of 17,893 women. Women were offered HIV testing and nevirapine as indicated by the standard PMTCT protocol. The HIV prevalence among women attending the clinics was 2.2% (range = 0.3–5.5%), which was similar to other estimates of HIV seroprevalence in Kinshasa.25

Standard practice in Kinshasa is to provide IPTp for malaria with two doses of sulfadoxine-pyrimethamine to all pregnant women, with a third dose for HIV-positive women. Clinic-level data on the number of women receiving each dose were used; the base-case likelihood was estimated to be the mean for all of the clinics (78.3% for the first dose and 50.9% for the second dose), with the range across clinics used in sensitivity analyses. Because data were not available by HIV status, we estimated the compliance with the third dose among HIV-positive women as the number of women receiving third doses divided by the number of HIV-positive women seen by the clinic: 39.4% received all three doses of IPTp (range 0% [4 clinics] to 100% [4 clinics]).

Women could choose to use the ITN provided during pregnancy and during the infant’s first year of life. Questionnaires were used to measure adherence with ITN use among the women attending the Bomoi Antenatal Clinic in the N’Djili

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Base-case value (range†)</th>
<th>Data source</th>
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</thead>
<tbody>
<tr>
<td>Mother HIV-positive</td>
<td>2.1% (0.3–5.5%)</td>
<td>28 ANCsc</td>
</tr>
<tr>
<td>Infant mortality rate (per 1,000)</td>
<td>95 (83–129)</td>
<td>9–11</td>
</tr>
<tr>
<td>RR (maternal HIV+ vs. HIV−)</td>
<td>3.08 (95% CI = 1.51–6.23)</td>
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<tr>
<td>RR (maternal HIV+ vs. HIV−)</td>
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<tr>
<td>Low birth weight rate (per 1,000)</td>
<td>120 (92–164)</td>
<td>Bomoi13,14</td>
</tr>
<tr>
<td>RR (maternal HIV+ vs. HIV−)</td>
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<tr>
<td>RR (maternal HIV+ vs. HIV−)</td>
<td>0.72 (95% CI = 0.53–0.98)</td>
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<tr>
<td>Stillbirth rate (per 1,000)</td>
<td>56 (42–70)</td>
<td>Bomoi ANC27</td>
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<tr>
<td>RR (maternal HIV+ vs. HIV−)</td>
<td>2.7 (95% CI = 1.3–5.5)</td>
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<tr>
<td>RR (maternal ITN vs. no ITN) (first–fourth pregnancy)‡</td>
<td>0.67 (95% CI = 0.47–0.97)</td>
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<td>HIV transmission to infant by one year of life</td>
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<tr>
<td>Mother did not receive nevirapine</td>
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<td>Mother received nevirapine</td>
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<td>Adherence to ITN by</td>
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<tr>
<td>Mother</td>
<td>85% (±10%)</td>
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<tr>
<td>Infant</td>
<td>63% (±10%)</td>
<td>Bomoi ANC</td>
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<tr>
<td>Adherence to IPTp</td>
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<tr>
<td>First dose (HIV+/HIV−)</td>
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<td>Second dose (HIV+/HIV−)</td>
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<tr>
<td>Third dose (HIV+ only)</td>
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<td>PMTCT received</td>
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<tr>
<td>Time with HIV (in months)</td>
<td>13.9</td>
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<tr>
<td>Time with AIDS (in months)</td>
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<td>Disability weight (AIDS)</td>
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<td>Costs per ITN (in 2005 US $)</td>
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<td>ITN purchase and transport to Kinshasa</td>
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<td>Training for providers</td>
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<tr>
<td>Distribution within clinic</td>
<td>$0.011 ($0.003–$0.019</td>
<td>Program</td>
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</table>

*RR (maternal HIV+ vs. HIV−) = relative risk of the third dose among HIV-positive women as the number of women receiving third doses divided by the number of HIV-positive women seen by the clinic: 39.4% received all three doses of IPTp (range 0% [4 clinics] to 100% [4 clinics]).
†RR (maternal HIV+ vs. HIV−) = relative risk of the third dose among HIV-positive women as the number of women receiving third doses divided by the number of HIV-positive women seen by the clinic: 39.4% received all three doses of IPTp (range 0% [4 clinics] to 100% [4 clinics]).
‡For women of parity 1–2 who do not receive a full course (i.e., two doses for HIV− women and 3 doses for HIV+ women) of IPTp and who use ITNs; otherwise used for women of parity 3–4 who used ITNs.
†RR (maternal ITN vs. no ITN) = relative risk of the third dose among HIV-positive women as the number of women receiving third doses divided by the number of HIV-positive women seen by the clinic: 39.4% received all three doses of IPTp (range 0% [4 clinics] to 100% [4 clinics]).
Health Zone. Bomoi Antenatal Clinic, administered by the Salvation Army, is the largest clinic, attending an average of 320 new pregnant patients each month. A baseline questionnaire was administered to 360 women chosen randomly from the first 1,000 women who received ITNs. A second questionnaire was administered in the postpartum ward at delivery (32 women were lost to follow-up) and a third questionnaire was administered during a home visit 6 months postpartum to 103 women chosen randomly from the initial 360 women. At the time of delivery and at 6 months postpartum, 85% and 84% of women, respectively, responded that they slept under the bed net everyday or almost everyday during the past month. At 6 months postpartum, 63% of women reported that the child slept under the ITN the previous night. Interviewers also observed that 70% of households had the ITN hanging in the correct position during the home visit. Women in the study washed the nets a maximum of eight times.

**Health outcomes. Stillbirths and LBW infants averted.** We used the stillbirth rate among women attending the Bomoi Antenatal Clinic (5.6%) as the base-case, or most likely, scenario. The minimum value was derived from 2001 data for the DRC.13 Because we used stillbirth rates from Kinshasa, where IPTp is considered standard of care, we did not adjust the stillbirth rates for IPTp use. We did adjust the stillbirth rate up or down depending on the mother’s HIV status using data from Kenya.14 In addition, we adjusted for the effect of ITN use during pregnancy for women in their first and second pregnancies who did not receive a full course of IPTp.16 Because women in their third and fourth pregnancies who used their ITNs were assumed to receive benefits from the ITNs but not IPTp,26 we adjusted their stillbirth rate. For women of parity greater than 4, we assumed no benefit from the ITNs,1 but did assume a protective effect for their live-born infants.

The base-case rate for LBW (i.e., birth weight < 2,500 g) was that rate reported by the United Nations Children’s Fund for the DRC.13 For the minimum and maximum rates, we used the rates among women attending the Bomoi Antenatal Clinic and for Maniema, DRC,14 respectively. Because numerous studies have shown that the prevalence of LBW is higher in infants born to HIV-positive mothers,15,27,28 we adjusted the rates of LBW up or down depending on the mother’s HIV status. As we had done for stillbirth rates, we adjusted the LBW rates for ITN use in the following way. For women of first or second parity who did not receive a full course of IPTp but used the ITN during pregnancy, we accounted for the protective effect of the ITN, women (first or second parity only) who received a full course of IPTp and used their ITNs did not receive any additional protection from the ITN.

**Infant deaths averted.** As the base-case, we used the infant mortality rate of 95 per 1,000 for urban DRC,6 with minimum and maximum values corresponding to the rates for Kinshasa15 and all of the DRC,11 respectively. The infant mortality rate was adjusted to reflect the protective efficacy of ITN use during the first year of life and to account for increased risks of infant mortality associated with LBW and HIV status using data from Malawi.12 The protective efficacy of ITN use was based on an efficacy study in Kenya,7 which also has perennial malaria transmission.

**Life-years and disability-adjusted life-years.** The HIV-negative children who survived the first year of life were assumed to survive an additional 49.8 years, the life expectancy at ages 1–4 in the DRC.25 The HIV-positive children who survived beyond the first year of life were assumed to survive 22.9 months.25 We combined life expectancy with health state valuations (i.e., weights associated with illnesses and conditions) to calculate DALYs. Age-specific health state valuations from the World Health Organization’s Choosing Interventions that are Cost Effective (CHOICE program)29 were combined with life expectancy for HIV-negative children. For children with HIV and/or acquired immunodeficiency syndrome, health state valuations were calculated as one minus the disability weight associated with a particular health state.22

**Costs.** We used a health provider perspective, estimating the cost of ITN distribution using program records. Costs include the cost of the ITNs, transport of ITNs to Kinshasa, storage of ITNs, transportation of ITNs within Kinshasa, staff training, and staff wages for distribution (Table 1). All costs are expressed in 2005 US dollars. The Global Fund donated the ITNs at $8 each, inclusive of shipping and customs; in sensitivity analysis, we used estimates obtained directly from the manufacturer (US $6.01). Clinic administrators provided wages for staff ranging from US $0.174 to US $1.15 per hour. These wages for persons involved in the program include salary and benefits. Health care costs (i.e., medications, clinic visits, and hospitalizations) averted by the intervention were not included in the model, nor were changes in total health care costs because of survival of infants.

**Analyses.** Cumulative costs, numbers of infant deaths, LYs, and DALYs were estimated with and without the ITN program. The difference in cost was divided by the difference in outcomes to calculate the incremental cost-effectiveness ratios (ICERs) in US dollars per infant death averted, LY saved, and DALY averted. Costs and outcomes occurring beyond the first year were discounted to the beginning of the model at 3% per year.30,31 The primary or base-case analysis was performed for all women.

We conducted both one-way and probabilistic sensitivity analyses to account for differences at the 28 antenatal clinics and in the data used in the decision model.30,32,33 One-way (deterministic) sensitivity analyses were used to assess the robustness of our findings to variations in individual model parameters. To do this assessment, we varied key model parameters across plausible values one at a time and examined the corresponding effects on the ICERs. Simulations also were performed to estimate outcomes and cost-effectiveness ratios for two additional distribution schemes: 1) women of first or second parity only (i.e., a situation of extreme resource constraints) and 2) women of first through fourth parity (i.e., resource constraints less dire than under the first scenario). In these scenarios, we would have distributed ITNs to 9,483 and 14,851 women, respectively, and thus apportioned the costs of ITN transport, security, and storage; staff training; and distribution costs across these reduced number of ITNs. That is, cost per ITN for women of first or second parity only and first through fourth parity only were US $10.87 and US $9.83, respectively.

To assess parameter uncertainty, probabilistic sensitivity analyses were conducted using Monte Carlo simulation (2,000 iterations). All simulations were conducted using Crystal Ball version 7.3.1 (Decisioneering, Oracle, Denver, CO). Risks or probabilities were modeled using beta distributions and relative risks with the lognormal distribution.34 Where ranges of input values (e.g., 95% CIs or multiple sources of data) were unavailable from the literature or program records, we assigned plausible ranges of ±10% of the base-case values.
Results of these simulations are depicted in an incremental cost-effectiveness plane that demonstrates the likelihood that adding ITNs is cost-effective for values that a decision maker would be willing to pay to avoid an additional DALY. Typically, any intervention with an ICER less than the per capita gross domestic product (GDP) per DALY averted (in the case of the DRC, US $700/DALY averted) would be considered highly cost-effective. Interventions having ICERS above that level but less than three times the GDP per capita/DALY were considered worthwhile or cost-effective. However, it is reasonable to argue that a low- or middle-resource country might not consider spending that much for a medical intervention given competing priorities. Thus, we often compare our ICERS to a lower threshold, the per capita health care expenditure (i.e., in the DRC, US $15/DALY averted), under the assumption that doing so is more likely to place the intervention into an appropriate context. In the analyses presented here, we compare our results to both thresholds.

RESULTS

Adding ITN distribution at 28 antenatal clinics in Kinshasa is estimated to have yielded 414 fewer infant deaths (2,165 versus 1,751) and 587 fewer LBW deliveries (3,140 versus 3,727), save 10,855 life-years, and avert 9,897 DALYs compared with the standard antenatal services (Table 2). The additional costs of the program were estimated to be US $170,423, or US $9.52 per ITN distributed. The cost-effectiveness ratios for our base-case scenario were US $411.13 per infant death prevented, US $15.70 per LY saved, and US $17.22 per DALY averted. Of the infant deaths averted, 247 were among women carrying their first or second pregnancy, 149 were among women carrying their third or fourth pregnancy, and 18 were among women carrying their fifth or greater pregnancy. The distribution of parities in our study was 53% first or second pregnancy, 30% third or fourth pregnancy, and 18% among women carrying their fifth or greater pregnancy. The distribution of parities in our study was 53% first or second pregnancy, 30% third or fourth pregnancy, and 18% fifth or greater pregnancy.

Our simulations of different distribution schemes (Table 2), despite increased costs per ITN, remained highly cost-effective compared with the commonly accepted threshold of one times the GDP per DALY averted (i.e., US $700/DALY averted) and was just slightly higher than our proposed lower threshold of the per capita health expenditures (US $15/DALY averted). Finally, because malaria parasitemia is so high in Kinshasa despite use of IPTp (60% of women were positive during pregnancy), we modeled a scenario in which women of first or second parity who received a full IPTp course and used their ITNs during pregnancy had reduced stillbirth and LBW rates as a result of using the ITN. The incremental cost-effectiveness ratio continued to be highly cost-effective at US $16.93/DALY averted (compared with a base-case of US $17.22/DALY).

Results of probabilistic analyses are plotted in the incremental cost-effectiveness plane (Figure 1). All points lie in the quadrant where providing ITNs is more costly and more effective. All 1,000 points lie to the right and below the $700/DALY averted threshold, thus suggesting that adding ITNs would be considered highly cost-effective. The dashed line indicates the threshold ICER of $15/DALY (the per capita health care expenditure in the DRC); 492 of the 1,000 simulation results lie below or to the right, suggesting that adding ITNs would be cost-effective at this reduced threshold. The cost-effectiveness acceptability curve (Figure 2) indicates that there is a 49.2% likelihood that providing ITNs to all women regardless of parity is cost-effective at a threshold of US $15.00/DALY. At US $36.02/DALY, a decision maker would have a 1% chance of making the wrong decision by adding ITNs; at US $106/DALY, adding ITNs is always cost-effective.

Systematic variation of individual model parameters in one-way sensitivity analyses (Table 3) indicates that the model is most sensitive to variations in the relative risks of stillbirth and infant mortality associated with ITN use, the relative risk of infant mortality associated with LBW, the incidence rates of stillbirths and infant mortality, and the cost of the ITNs. The results of the one-way sensitivity analyses were similar regardless of outcome measure examined. Purchasing ITNs directly from the manufacturer improved the cost-effectiveness to US $13.62/DALY averted, US $325.23/death averted, and US $12.42 per life-year saved.

DISCUSSION

Distribution of ITNs at 28 antenatal clinics in Kinshasa prevented an estimated 414 infant deaths. From the health provider perspective, it costs US $411.13 per infant death prevented, US $15.70 per life-year saved, and US $17.22 per DALY averted. Our results are more favorable than results previously reported for ITN distribution through a social marketing program (US $873 per child death averted) and compare favorably with distribution alongside a measles vaccination program (US $635 per child death averted, US $16 per DALY averted). Our results also compare favorably with other preventive measures, for example, U.S. $84 per DALY averted for PMTCT with nevirapine, US $2 to US $17 per DALY averted for ITNs for measles vaccination, and more than US $2,000 per DALY averted for hypertension management.

Distribution at the antenatal clinic benefits not only the pregnant woman, but also the infant, because of use by the mother-infant pair after delivery. Also, distribution alongside PMTCT services facilitates ITN access for HIV-positive pregnant women, who have greater morbidity from malaria than their HIV-negative counterparts.
We found that this program is the most cost-effective for women of lower parity (who with their infants are at greater risk of malaria sequelae), whereas benefits were lower for those women carrying their fifth or greater pregnancy. This phenomenon may be explained by the lack of effect of ITNs in reducing stillbirths and LBW deliveries after the fourth pregnancy. In this case, the benefits are primarily to the infant who sleeps under the ITN during the first year of life. Under extremely resource-constricted circumstances, when perhaps it may be conceivable to prioritize distribution of ITNs to women in their first through fourth pregnancies or even to women in their first or second pregnancies, the intervention remains cost-effective.

We believe our analysis is conservative because we account only for infant mortality and do not account for the cost savings associated with a reduction in LBW deliveries or malaria cases averted in mothers or infants. For example, we do not account for health care use that would result from LBW or
its sequelae. Also, we do not account for costs saved because of fewer medications used and less frequent clinic visits and hospitalizations for malaria. Currently in the DRC, 68% of outpatient visits and 30% of hospitalizations are estimated to be caused by malaria. Because ITN use by children reduces rates of uncomplicated malaria by 50% and severe malaria by 45%, the cost-savings from decreased use of health services and medications is likely to be substantial.

A limitation of the study is that it simulates results for a single region, an urban environment, in the DRC. In particular, we measured ITN adherence at one typical clinic in Kinshasa, rather than in all 28 clinics involved in the original ITN distribution program. Thus, the observed adherence may be generalizable to many clinics in the capital, but may not reflect adherence in rural areas or in other urban areas in the DRC. To address this limitation, we use and describe sensitivity analyses, which may permit wider applicability of our results. We also were unable to directly measure health outcomes (i.e., stillbirths, LBW deliveries, and vertical HIV transmission) for the women who received ITNs from our program. Instead we used outcomes data from the peer-reviewed literature and used sensitivity analysis to evaluate the effect of using these alternative data. Finally, we assumed that adherence with ITN use would stay the same from 6 months postpartum, when it was measured, until 12 months postpartum, the end of our time frame for outcomes. Although ITN use may decrease over time, Lindblade and others reported that ITN use increased during the course of the study, possibly because ITN use became more culturally acceptable.

The adherence with ITN use by the mothers and their infants in our study was somewhat higher than reported in the recent literature. Yukich and others reported ITN use in children less than five years of age ranging from 13.9% to 56% compared with 85% reported by mothers in our study at delivery. Had we used these lower rates, our incremental cost-effectiveness ratios would have been US $18 to US $22 per DALY. Had we used these lower rates, our incremental cost-effectiveness ratios would have been US $18 to US $22 per DALY.

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