Cost-effectiveness of parenteral artesunate for treating children with severe malaria in sub-Saharan Africa

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Objective To explore the cost-effectiveness of parenteral artesunate for the treatment of severe malaria in children and its potential impact on hospital budgets.

Methods The costs of inpatient care of children with severe malaria were assessed in four of the 11 sites included in the African Quinine Artesunate Malaria Treatment trial, conducted with over 5400 children. The drugs, laboratory tests and intravenous fluids provided to 2300 patients from admission to discharge were recorded, as was the length of inpatient stay, to calculate the cost of inpatient care. The data were matched with pooled clinical outcomes and entered into a decision model to calculate the cost per disability-adjusted life year (DALY) averted and the cost per death averted.

Findings The mean cost of treating severe malaria patients was similar in the two study groups: 63.5 United States dollars (US$) (95% confidence interval, CI: 61.7–65.2) in the quinine arm and US$ 66.5 (95% CI: 63.7–69.2) in the artesunate arm. Children treated with artesunate had 22.5% lower mortality than those treated with quinine and the same rate of neurological sequelae: (artesunate arm: 2.3 DALYs per patient; quinine arm: 3.0 DALYs per patient). Compared with quinine as a baseline, artesunate showed an incremental cost per DALY averted and an incremental cost per death averted of US$ 3.8 and US$ 123, respectively.

Conclusion Artesunate is a highly cost-effective and affordable alternative to quinine for treating children with severe malaria. The budgetary implications of adopting artesunate for routine use in hospital-based care are negligible.

Abstracts in عربي, 中文, Français, Русский and Español at the end of each article.

Introduction

Despite reported falling transmission in much of sub-Saharan Africa,[1–3] malaria remains a leading cause of inpatient admissions and mortality in paediatric wards.[4–6] The policy for first-line treatment of severe malaria is a critical factor in determining malaria mortality. The choice of treatment must ultimately be dictated not only by its efficacy, but also by the ability of frail health systems to sustain its routine use. In much of sub-Saharan Africa, per-capita health expenditure remains extremely low, with annual government health expenditure per capita averaging 34 United States dollars (US$).[7] The cost of inpatient care for a case of severe malaria has been estimated at between US$ 12 and US$ 75 and this poses a considerable burden on limited resources.[4,8]

Quinine remains the mainstay treatment of severe malaria in sub-Saharan Africa. Parenteral quinine costs as little as US$ 0.27 per ampoule[9,10] and is widely available in health facilities across the continent. It is administered either intramuscularly or intravenously, three times per day. As an infusion quinine must be given over several hours and although it is well absorbed when given intramuscularly, this route can cause abscesses and sciatic nerve damage and has been associated with tetanus.[11] Artesunate is a more expensive drug, costing around US$ 1.06 per vial. However, it is only administered once daily and can be given as an intravenous bolus injection or by intramuscular injection. It has also been shown to be safe and well tolerated.[12]

Artesunate has previously been shown not only to be more effective for the treatment of severe malaria in adults in Asia, but also highly cost-effective, with a cost per death averted of just under US$ 150.[10] Whether these findings are transferable to children in Africa, among whom the largest share of malaria mortality occurs, remains to be explored. The African Quinine Artesunate Malaria Treatment (AQUAMAT) trial is the largest hospital-based clinical trial for severe malaria to date.[13] It was carried out in 11 sites in 9 countries across sub-Saharan Africa and recruited children with severe malaria who were randomized to receive either parenteral quinine or artesunate. Parenteral treatment was completed with a course of oral artemisinin combination therapy. The primary outcome measure was in-hospital

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Table 1. **Sites included in the African Quinine Artesunate Malaria Treatment trial**

Site[a]	Region of Africa	Malaria endemicity	Hospital level
Korogwe, United Republic of Tanzania	Eastern	Endemic and perennial with seasonal peaks/Low	Primary (district hospital)
Teule, United Republic of Tanzania	Eastern	Endemic and perennial with seasonal peaks/High	Secondary (district hospital)
Mbarara, Uganda	Eastern/Central	Endemic and perennial with seasonal peaks/High	Tertiary
Ilorin, Nigeria	Western	Endemic and perennial with seasonal peaks/High	Tertiary
Mozambique	Southern	Endemic and perennial with seasonal peaks/High	Tertiary
Gambia	Western	Endemic with seasonal transmission/High	Tertiary
Ghana	Western	Endemic and perennial with seasonal peaks/High	Tertiary
Kenya	Eastern	Endemic and perennial with seasonal peaks/Low	Secondary (district hospital)
Rwamagana, Rwanda	Eastern	Endemic and perennial with seasonal peaks/Low	Secondary (district hospital)
Niyanza, Rwanda	Eastern	Endemic and perennial with seasonal peaks/Low	Secondary (district hospital)
Democratic Republic of the Congo	Central	Endemic and perennial with seasonal peaks/High	Secondary (district hospital)

[a] The top four sites were included in the costing analysis.

mortality, with neurological disability assessed at 28 days as an important secondary outcome.

This economic analysis was conducted alongside the AQUAMAT clinical trial to explore the cost-effectiveness of artesunate for the management of severe malaria in children in sub-Saharan Africa. The budget impact of the use of artesunate was also estimated to assess its affordability in routine practice.

Methods

Evaluation framework

A provider perspective was taken, being most relevant to the context of inpatient care. This perspective accounts for all resources used in health facilities for the treatment of severe malaria as well as for mortality and disability among the patients. The evaluation framework is a cost-effectiveness analysis using cost per disability-adjusted life year (DALY) averted and cost per death averted as measures of cost-effectiveness.

When one drug is more expensive and more effective than its comparator, the incremental cost per DALY averted is calculated. This ratio is compared with a decision threshold that is assumed to convey the maximum policy-makers are willing and able to pay for an additional DALY averted. The baseline decision thresholds used as a reference are the conservative estimates of US$ 25 and US$ 150, as suggested by the World Health Organization (WHO) and the World Bank.[14,15]

Data collection

The study was conducted in four of the 11 AQUAMAT sites.[13] Two of the selected sites, Muheza and Korogwe, were in dif-

ferent areas of the United Republic of Tanzania. A third site was in Mbarara, Uganda, and a fourth in Ilorin, Nigeria. The sites were chosen to represent geographical and epidemiological diversity (Table 1). Medical resource use and cost data were collected between June 2009 and July 2010, when the last patient was recruited. Treatments, diagnostic tests and medical equipment used in the management of severe malaria were recorded for a total of 2300 patients.

The hotel costs of inpatient care (i.e. costs of capital, supportive departments and labour) were obtained from WHO's *choosing interventions that are cost-effective* (WHO-CHOICE) framework,[16] which stratifies costs by country and health facility level. The cost per inpatient day was multiplied by the patient length of stay. Drug costs were obtained from the *International drug price indicator guide* using the median buyer price.[9] Costs of laboratory tests were estimated using patient charges. All costs were calculated in US$ at 2009 prices; the WHO-CHOICE costs were obtained in 2005 local currency units, adjusted for inflation using the consumer price index and converted to US$ using the official average 2009 exchange rate.[17,18] Life-time costs associated with neurological sequelae were not included. Mortality and disability data were derived from the pooled estimates from all 11 sites in the AQUAMAT study.[13]

Model outline

A decision tree was constructed to depict the progression from severe illness treated with either artesunate or quinine (Fig. 1). Patients can enter either the quinine or artesunate arm, where they either survive or die according to the mortality

observed in the trial. The number of life years lost (YLL) for patients that die are calculated according to the patient's age and life expectancy at death. Surviving patients can either be cured or have mild, moderate or severe neurological sequelae. The years lived with disability (YLD) are calculated for patients with neurological sequelae. The percentages shown in Fig. 1 are the baseline mean estimates for each chance node. The model draws random samples from the data set with replacement (bootstrapping) to derive the costs and from assigned distributions for probabilities at each branch. The costs associated with each treatment include those for the antimalarials and other drugs, supportive treatment, diagnostic tests, treatment of adverse events and hotel costs for inpatient stay.

The primary measure of clinical outcome was the number of DALYs in each of the treatment arms. DALYs account for both YLL due to early mortality and YLD, calculated using standard methods.[19] The number of YLL for a patient that died was dependent on the average patient age and life expectancy in the four countries where the data were collected. This value was discounted using a baseline value of 3% annually.[20] Full age modulation was included in the baseline analysis, implying more conservative effectiveness gains.[19] Disability weights for patients with sequelae were based on their condition as documented on day 28 follow-up visits; disability weights were assigned using the Global Burden of Disease tables, as shown in Table 2.[21] Disability during the illness episode was not included, as this was assumed to be minor and equal between treatment arms and therefore to

Fig. 1. **Dendrogram showing clinical progression**
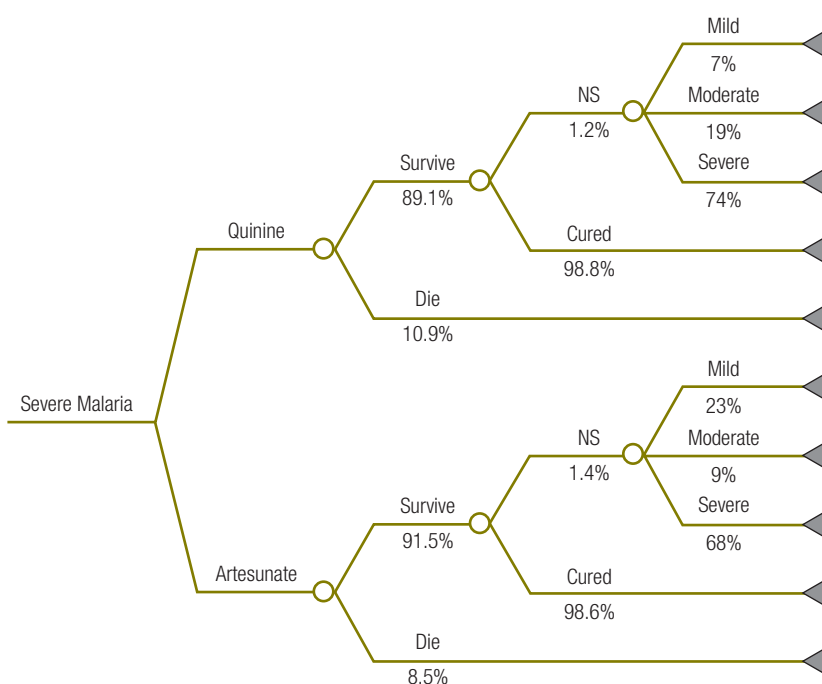
NS, neurological sequelae.

have no effect on the incremental advantage of either treatment.

The secondary measure of outcome was the incremental cost per death averted, calculated by multiplying the numbers needed to treat (NNT) to avert a death by the difference in treatment costs.

Sensitivity analyses

We used one-way sensitivity analyses for parameters whose estimates were not based on high-level evidence, or in cases in which the choice of parameter value was methodological. The discount rate varied between 0–10%, life expectancy was changed from local to global estimates, and the use of age modulation for the calculation of DALYs was omitted.[20] We did a threshold analysis for the drug costs at which the decision to adopt one intervention over the other is reversed.

We did a probabilistic sensitivity analysis for parameter uncertainty in cost and for clinical outcomes. The analysis was done in TreeAge Pro® by running the model 50 000 times, each time randomly selecting from the range of values for each parameter. For costs, the values were drawn from the database of patient

Table 2. **Disability weights, costs and analytical parameter values**

Parameter	Baseline estimate (distribution parameters or sensitivity analysis values)	Source
Mortality		
Quinine (pooled)	0.109 (β distribution; $\alpha = 167$; $\beta = 1\,357$)	Primary
Artesunate (pooled)	0.085 (β distribution; $\alpha = 264$; $\beta = 2\,847$)	
Neurological sequelae		
Quinine (pooled)	0.012 (β distribution; $\alpha = 21$; $\beta = 2\,692$)	Primary
Artesunate (pooled)	0.014 (β distribution; $\alpha = 22$; $\beta = 2\,690$)	
Disability weighting		
Mild neurological sequelae[a]	0.024	[21]
Moderate neurological sequelae[b]	0.248	[21]
Severe neurological sequelae	0.471	[21]
Costs		
Hotel (2009 US$ per day)		
Ilorin, Nigeria	18.9	[16]
Mbarara, Uganda	7.7	[16]
Muheza, United Republic of Tanzania	7.4	[16]
Korogwe, United Republic of Tanzania	5.7	[16]
Quinine dihyrocholride (300 mg/ml, 2 ml ampoule) cost (US$)	0.27	[9]
Artesunate (60 mg vial, 1 ml ampoule) cost (US$)	1.06	[9]
Analytical values		
Decision threshold (US$)	150 (25–880)	[14,15]
Annual discount value (%)	3 (0–10)	[19]
Age modulation	1 (0)	[19]

US$, United States dollar.
[a] Based on weighting for cognitive impairment following meningitis.
[b] Based on motor impairment following meningitis.

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Table 3. Mortality and incidence of moderate or severe neurological sequelae

Parameter	Quinine	Artesunate
Mortality	297/2713 (10.9%)	230/2712 (8.5%)
Severe neurological sequelae	21/2713 (0.8%)	22/2712 (0.8%)
DALYs	3 (95% PI: 2.4–4.6)	2.3 (95% PI: 1.9–2.6)[a]
Incremental DALYs averted with the use of artesunate	–	0.7 (95% PI: 0.2–1.3)[a]
Incremental number needed to treat (with artesunate) to avert 1 death	–	41 (95% CI: 25–112)

CI, confidence interval; DALY, disability-adjusted life year; PI, percentile interval.

[a] The 95% PI represents the interval between the 2.5% and 97.5% percentiles.

costs. For clinical outcomes, β distributions were calculated from the incidence of mortality and neurological sequelae in surviving patients in all AQUAMAT study sites and were converted in the model to DALYs. The measure of dispersion reported for DALYs are the values for the interval between the 2.5% and 97.5% percentiles, defined here as the 95% percentile interval (95% PI).[22]

The incremental cost-effectiveness ratio was compared against a range of thresholds for policy-makers' willingness to pay for the additional health benefit. This was summarized using cost-effectiveness acceptability curves, indicating the probability that the intervention is cost-effective given the uncertainty surrounding the model parameters across a range of willingness-to-pay thresholds.[22]

Budget impact analysis

The annual costs of treating all paediatric malaria admissions with artesunate rather than quinine over one year were calculated based on the cost of inpatient care multiplied by the annual number of severe malaria admissions in the four study sites. Costs were also calculated with the exclusion of hotel costs (overheads and labour), which are not immediately affected by the choice of antimalarial drug treatment. The annual number of severe malaria admissions in each site was obtained from hospital records for 2008, apart from Korogwe, where these data were not available. For Korogwe the number of admissions in the AQUAMAT trial was used instead.

Ethical approval

Ethical approval for the AQUAMAT trial was obtained from the Oxford Tropical Research Ethics committee and from the ethical review board in each site individually. Further approval was granted for the retrospective collection of cost data from the patients medical files.

Results

In 5425 patients enrolled in the main trial, mortality in the quinine arm was 10.9% compared with 8.5% in the artesunate arm – a 22.5% (95% CI: 8.1–36.9%) reduction. The NNT with artesunate to avert a death was 41 (95% CI: 25–112). There was no significant difference in the rate of neurological sequelae between the two arms. Combining the differences in rates of mortality and neurological sequelae between treatment arms, an additional 0.7 (95% PI: 0.2–1.3) DALYs per patient were averted with artesunate by comparison with quinine (Table 3).

The costs of treatment were very similar between the two arms, as shown in Table 4, with a mean of US$ 66.5 (95% CI: 63.7–69.2) in the artesunate arm and only US$ 3 less in the quinine arm, at US$ 63.5 (95% CI: 61.7–65.2).

The hotel costs constituted approximately half the total cost and were significantly higher in Ilorin, a tertiary hospital, than in other hospitals. The mean number of hospitalization days was slightly lower in the quinine arm, partly resulting from higher mortality rates early after admission.

The average cost of a full treatment course of quinine, until the patient was able to take oral medication, was just over US$ 1.3 (95% CI: 1.25–1.34), compared with an average cost of US$ 3.3 (95% CI: 3.2–3.4) in patients treated with artesunate. Costs for intravenous fluids were slightly higher in the quinine arm, in part because quinine administered intravenously is given as an infusion, whereas artesunate is administered as a bolus injection.

Given these costs and outcomes, the incremental cost per DALY averted when using artesunate rather than quinine was US$ 3.8 and the incremental cost per death averted was US$ 123 ($95% CI: 75–336). The results for individual study sites are shown in Table 5.

Sensitivity analysis

Results were not sensitive to the parameters used in converting YLL and YLD to DALYs. Whether no discounting was applied or with a 10% discount value; with either global or local life expectancy estimates; and with and without the age modulation, the incremental cost-effectiveness ratio varied between US$ 2.9 and US$ 4.3 per DALY averted.

A threshold analysis determined that, assuming even a conservative willingness to pay of US$ 150 per DALY averted, artesunate could cost up to US$ 105 per full treatment course before it ceased to be cost-effective. Although parenteral quinine is cheap, it comprises only a small fraction of the total costs of inpatient care. Even if quinine were obtained at no cost, this would not reverse the direction of the cost-effectiveness results. Fig. 2 illustrates the relatively tight distribution for total cost of care which clustered closely around the mean values and almost never approached the threshold value above which artesunate ceased to be cost-effective.

The probabilistic sensitivity analysis explored the uncertainty surrounding the cost and clinical outcomes observed in the trial. Fig. 3 shows the cost-effectiveness acceptability curve. At the very outset, when policy-makers are assumed not to be willing to pay anything for further health gains, the probability that either treatment would be cost-effective is almost equal at 50%. If, however, policy-makers are willing to pay up to US$ 25 for an additional DALY averted (the lowest benchmark commonly used in economic evaluation in the context of low income countries), artesunate appears to be more cost-effective with a probability of almost 80%. This probability exceeds 95% as the willingness to pay increases to the next commonly used threshold of US$ 150.

Table 4. **Mean malaria inpatient treatment costs (in United States dollars, US$) in each study arm according to cost category and study site**

Cost category	Teule		Korogwe		Mbarara		Ilorin		All sites	
	QNN	ART	QNN	ART	QNN	ART	QNN	ART	QNN	ART
Trial drug	1.2 (1.8)[a]	2.8 (4.1)	1.6 (2.8)	3.5 (6.4)	1.2 (2.0)	3.7 (6.2)	1.2 (1.3)	3.5 (3.2)	1.3 (2.0)	3.3 (4.9)
Drugs	3.4 (5.1)	3.4 (5.0)	3.8 (6.8)	3.4 (6.2)	1.9 (3.2)	1.6 (2.6)	3.2 (3.7)	2.7 (2.4)	3 (4.7)	2.9 (4.3)
Fluids	12.3 (18)	12.2 (18)	16.7 (30)	12.3 (22)	13.1 (22)	12.5 (20)	11.6 (13)	13.6 (12)	13.5 (21)	12.5 (18)
Laboratories	18.4 (28)	18.2 (27)	10.5 (18)	10.4 (19)	5.9 (10)	5.9 (9.8)	3.5 (4.0)	4.9 (4.5)	11.6 (18)	11.5 (17)
Hotel	30.2 (46)	30.1 (45)	23 (41)	24.4 (45)	36.5 (62)	35.9 (60)	66.7 (77)	84 (77)	34.1 (53)	36.3 (54)
Total	65.5 (100)	66.7 (100)	55.6 (100)	54 (100)	58.6 (100)	59.6 (100)	86.2 (100)	108.7 (100)	63.5 (100)	66.5 (100%)

ART, artesunate; QNN, quinine.
[a] The figures in parentheses represent the percentage of total costs.

Budget impact

The predicted impact on the study hospital annual budgets of switching from parenteral quinine to artesunate is minimal, or even cost-saving (Table 6). Accounting for direct expenditure on drugs and other medical equipment, the impact ranged from an annual cost-saving of approximately US$ 500 in Korogwe to just under US$ 4000 in Nigeria. If overhead costs for inpatient care are included, the additional expenditure per annum in the Nigerian centre is much higher – just over $16 000. This is due to the survival benefit conferred by artesunate and the high costs per inpatient day incurred in this tertiary teaching hospital.

Discussion

This analysis shows that the cost of averting malaria-related deaths in sub-Saharan Africa by switching from quinine to artesunate was extremely low, with a mean value of US$ 123 per death averted. The results are similar to the incremental cost per death averted in adult Asian patients, which was estimated as US$ 148. Similarly, the cost per DALY averted with artesunate was only US$ 3.8, far below any of the commonly used willingness-to-pay thresholds. The cost-effectiveness acceptability curve suggested that the probability of artesunate being cost-effective is approximately 50% without any additional investment, and exceeded 95% at a willingness to pay of US$ 150. This compares very favourably with other interventions, such as the use of insecticide-treated nets, with a cost per death averted of US$ 254 to US$ 3437.[23] In addition, provided the drug is available, the use of artesunate is relatively easy to implement in any hospital setting.

While cost-effectiveness is an informative criterion for policy-makers considering the adoption of a new intervention, affordability must also be demonstrated, particularly in the highly constrained health systems present in many sub-Saharan African countries. The large number of malaria admissions implies that any change in treatment strategies could have a substantial impact on frail health systems. We have demonstrated that the use of artesunate is not only highly cost-effective but also entirely affordable, having a minimal impact on hospital budgets and in some instances being cost-saving. Even if the proportion of severe malaria cases reaching health facilities were to increase, this would most likely remain an affordable intervention.

Limitations

The analysis was carried out from the provider perspective, although inclusion of household costs would have had either no impact or would have favoured artesunate further. A broader societal perspective might also have accounted for the possibility of artemisinin resistance emerging following widespread use of artesunate.[24] This was not considered a high priority, as parenteral artesunate is provided only to patients with severe illness – a small fraction of the total number of antimalarial treatments used every year. Furthermore, almost all patients treated for severe malaria receive an effective oral combination therapy following treatment with the parenteral drug, reducing the likelihood of the development of resistance.[25]

We did not include the nursing time associated with administrating drugs. We also excluded the cost of consumables such as syringes, needles, cannulas and infusion sets because of the difficulty in collecting these reliably and their relatively low cost. Both these labour and consumables costs are likely to be marginally higher with quinine than artesunate, because quinine is given 3 times per day and as an infusion requires extra consumables and careful monitoring. Their inclusion would therefore further enhance the cost-effectiveness of artesunate. Reducing nursing time can improve the care for other patients and in the long run could have a potential impact on hospital budgets.

The costs of changing drug policy were excluded, but as a one-off cost spread over the expected lifetime of the policy change, the impact on the incremental cost-effectiveness ratio would be minimal. In some instances patient charges were used as proxies for costs. In practice, charges may not reflect actual economic costs. This has no effect on the incremental cost-effectiveness ratio as these items, mostly laboratory tests, were equally distributed in the trial arms.

There were several methodological limitations. While the use of DALYs allows for comparison of cost-effectiveness estimates for different health conditions and interventions, it is not without its limitations.[19,26,27] The use of age modulation, discounting, and global life expectancies has been criticized. In

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Table 5. **Cost[a] per disability-adjusted life year (DALY) averted and cost per death averted in each of the study sites**

Parameter	United Republic of Tanzania		Mbarara, Uganda	Ilorin, Nigeria	All sites
	Muheza	Korogwe			
Mean incremental cost per patient treated with artesunate	1.2	−1.6	1.0	22.5	3.0
Mean DALYs averted with artesunate	0.7 (pooled data from all trial sites)				
NNT[b] to avert 1 death	41 (pooled data from all trial sites)				
Cost/DALY averted	1.5	−2.0	1.2	28.1	3.8
Cost/death averted	49	−66	41	922	123

NNT, number needed to treat.

[a] All costs in United States dollars.

[b] This represents the number of patients one would need to treat with artesunate instead of quinine to avert 1 death.

this analysis we chose to adopt those methods and values that would imply the most conservative results in terms of the cost-effectiveness of artesunate. All these parameters were tested in the sensitivity analysis and showed only a minor impact on the results.

There was some variation in health outcomes and costs between the different sites, and therefore in their respective incremental cost-effectiveness ratios. The trial was powered to capture differences in effectiveness by pooling all sites. The main clinical analysis did, however, test for between-site heterogeneity and no significant variation was found. We therefore used the pooled estimate for clinical outcomes in our analysis. The main driver for the difference in costs was the overhead cost for inpatient stay, which was derived from the WHO-CHOICE framework rather than the primary costing of hospital overheads. Differences in overhead expenditure, however, are not as immediately affected by the choice of treatment as the variable expenditure on drugs and medical resources, and would materialize only when hospitals adjust their overhead expenditure to any changes in inpatient throughput.

Fig. 2. **Distribution of total treatment costs for severe malaria in four trial sites**
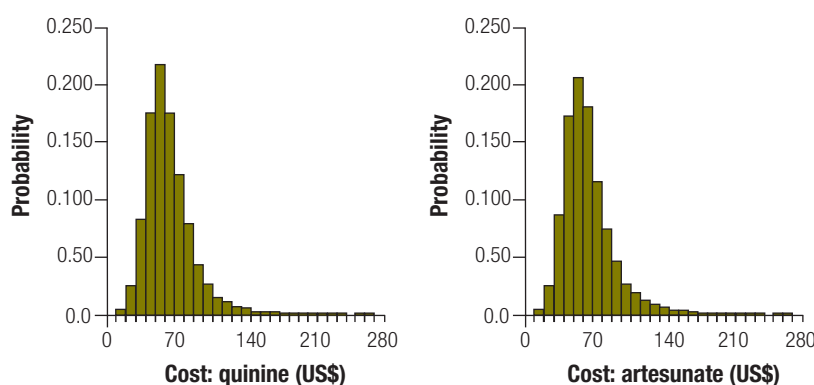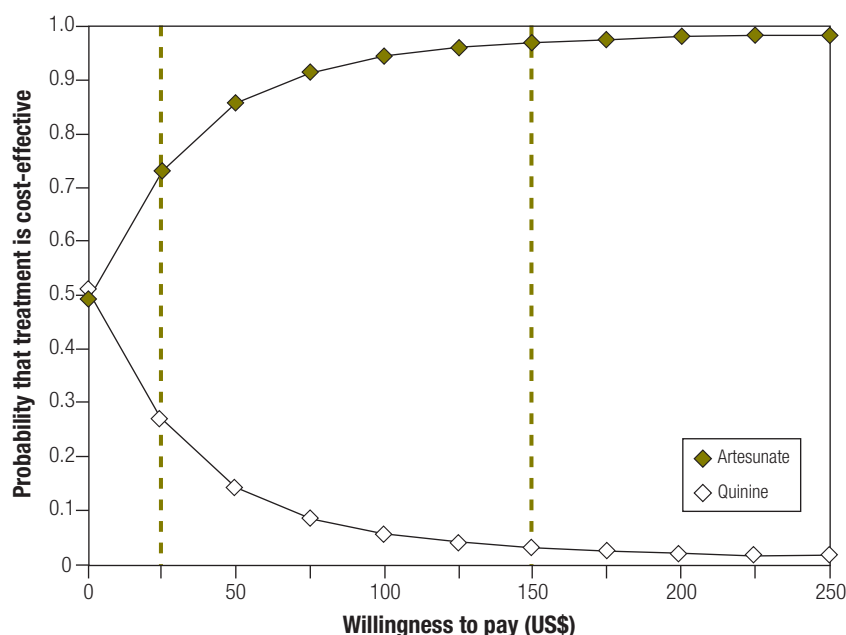

Fig. 3. **Cost-effectiveness acceptability curves for artesunate and quinine**

Conclusion

With this analysis we show that artesunate is effective, cost-effective and affordable, which stands as evidence to support its use in children with severe malaria in Africa.

The parenteral artesunate currently available on the market and used in this study does not yet have international drug regulatory authority registration, but WHO pre-qualification of the Chinese product was recently approved and the drug is licensed for use in many malaria-endemic countries and can be purchased with funds from the Global Fund to Fight AIDS, Tuberculosis and Malaria. A new formulation may be registered in the near future[28] and could be more expensive. However, this analysis has shown that even if the cost of artesunate were substantially higher, it would remain a cost-effective option. ■

Table 6. **Hospital admissions for severe malaria and impact on hospital budgets of switching from parenteral quinine to artesunate to treat severe malaria in childen**

Paremeter	United Republic of Tanzania		Mbarara, Uganda	Ilorin, Nigeria
	Muheza	Korogwe		
Patients admitted with severe malaria per year (No.)	555	169	584	708
Annual cost of switching to artesunate including hotel costs (US$)[a]	699	−271	526	16 142
Annual cost of switching to artesunate excluding hotel costs (US$)[b]	755	−509	876	3894

US$, United States dollar.

[a] Overhead costs for inpatient care as estimated in the WHO-CHOICE database.

[b] Only direct expenditure that will be affected by switching from quinine to artesunate.

مخلص

الفعالية لقاء التكلفة للأرتيزوينات المعطاة حقناً لمعالجة الأطفال المصابين ملاريا وخيمة في البلدان الواقعة جنوب الصحراء الأفريقية في أفريقيا

الغرض استكشاف الفعالية لقاء التكلفة للأرتيزوينات المعطاة حقناً لعلاج الملاريا الوخيمة في الأطفال وتأثير ذلك الضمني على ميزانيات المستشفيات. **الطريقة** أجرى تقييم لتكاليف الرعاية في المستشفى للأطفال المصابين ملاريا وخيمة في أربعة مواقع من 11 موقعاً أفريقياً مخصصة لتجربة علاج الملاريا بالكينين وبالأرتيزوينات، وذلك على أكثر من 5400 طفل. وقد جرى تسجيل الأدوية، والاختبارات المعملية، والسوائل المعطاة بالوريد المقدمة إلى 2300 مريض منذ دخولهم إلى المستشفى حتى خروجهم منها، كما سُجل طول مدد الإقامة في المستشفى لحساب تكلفة الرعاية في المستشفى. وجرى مطابقة المعطيات مع النتائج السريرية المجمعة وأدخلت في نموذج قرار لحساب التكلفة لكل سنة مصححة باحتساب مدد العجز الممكن تجنبها والتكلفة مقابل الوفاة الممكن تجنبها. **النتائج** كان متوسط تكلفة علاج الملاريا الوخيمة مشابهاً في مجموعتي الدراسة: 63.5 دولار أمريكي (فاصلة الثقة 95%: 61.7-65.2) في ذراع

الكينين، و 66.5 دولار أمريكي (فاصلة الثقة 95%: 63.7-69.2) في ذراع الأرتيزوينات. وكان معدل وفيات الأطفال المعالجين بالأرتيزوينات أقل مقدار 22.5% مقارنة ممن عولجوا بالكينين، وكان المعدل هو نفسه بالنسبة للعقابيل العصبية: (ذراع الأرتيزوينات: 2.3 من سنوات العمر المصححة باحتساب مدد العجز لكل مريض؛ وذراع الكينين: 3.0 من سنوات العمر المصححة باحتساب مدد العجز لكل مريض). وبالمقارنة مع الكينين كمستوى قاعدي، أظهرت الأرتيزوينات زيادة في التكلفة لكل سنة مصححة باحتساب مدد العجز ممكن تجنبها وزيادة في التكلفة مقابل كل وفاة ممكن تجنبها ممقدار 3.8 دولار أمريكي و 123 دولار أمريكي على التوالي. **الاستنتاج** تعد الأرتيزوينات فعالة للغاية لقاء التكلفة وبديلاً ميسوراً للكينين لمعالجة الأطفال المصابين ملاريا وخيمة. وتعد التبعات المالية لاستخدام الأرتيزوينات روتينياً في الرعاية داخل المستشفى عديمة الأهمية.

摘要

撒哈拉以南非洲地区运用注射青蒿琥酯治疗患有重症疟疾儿童的成本效益

目的 旨在探讨运用注射青蒿琥酯治疗患有重症疟疾儿童的成本效益以及该疗法对医院预算的潜在影响。

方法 非洲奎宁青蒿琥酯疟疾治疗试验涉及11个地点的5400多名儿童,本文评估了其中四个地点患有重症疟疾儿童的住院治疗成本。对2300名病人从住院到出院间的用药、化验和静脉注射液均进行了记录,同时还记录了住院天数以计算住院治疗成本。数据与所合并的临床结果相匹配并输入决策模型用以计算所避免的每个残疾调整生命年(DALY)的成本以及所避免的每例死亡的成本。

结果 两组研究小组中,治疗重症疟疾病人的平均成本类似:奎宁手臂注射为63.5美元(95%可信区间,CI: 61.7-65.2),青蒿琥酯手臂注射为66.5美元(95%可信区间,CI:63.7-69.2)。接受青蒿琥酯治疗儿童的死亡率比接受奎宁治疗儿童的死亡率低22.5%,而两种治疗方法的神经学后遗症相同(青蒿琥酯手臂注射:每病患2.3残疾调整生命年;奎宁手臂注射:每病患3.0残疾调整生命年)。与奎宁作为基线的情况相比,青蒿琥酯显示所避免的每一残疾调整生命年的增量成本和所避免的每例死亡的增量成本分别为3.8美元和123美元。

结论 青蒿琥酯是一种具有很高成本效益并且实惠的替代治疗重症疟疾儿童奎宁疗法的另类疗法。采用青蒿琥酯作为医院常规疗法的财政预算影响可以忽略。

Résumé

Rentabilité de l'artésunate parentéral administré chez les enfants gravement atteints de paludisme en Afrique subsaharienne

Objectif Étudier la rentabilité de l'artésunate parentéral dans le cadre du traitement d'enfants gravement atteints de paludisme et son impact potentiel sur les budgets hospitaliers.

Méthodes Les coûts des soins administrés aux patients hospitalisés gravement atteints de paludisme ont été évalués dans 4 des 11 sites participant à l'essai Traitement quinine/artésunate contre le paludisme en Afrique, réalisé sur plus de 5400 enfants. Afin de calculer le coût de l'hospitalisation, les médicaments, les essais en laboratoire et les liquides intraveineux administrés à 2300 patients entre leur admission et leur sortie ont été enregistrés, ainsi que la durée de l'hospitalisation. Les données ont été comparées avec les résultats cliniques regroupés et intégrés à un modèle de décision afin de calculer le coût par année de vie corrigée du facteur invalidité (AVCI) évité et le coût par décès évité.

Résultats Le coût moyen du traitement des patients gravement atteints du paludisme s'est révélé similaire dans les deux groupes expérimentaux:

63,5 dollars américains (US$) (intervalle de confiance 95% IC: 61,7–65,2) pour le bras recevant la quinine et 66,5 US$ (95% IC: 63,7–69,2) pour le bras recevant l'artésunate. Les enfants traités par artésunate affichaient un taux de mortalité inférieur de 22,5% à ceux recevant de la quinine, et un taux de séquelles neurologiques identique: (bras recevant l'artésunate: 2,3 AVCI par patient; bras recevant la quinine: 3,0 AVCI par patient). En comparaison avec la quinine en tant que ligne de base, l'artésunate a démontré un coût incrémental par AVCI évitée et un coût incrémental par décès évité de 3,8 US$ et 123 US$, respectivement.

Conclusion Dans le cadre du traitement des enfants gravement atteints de paludisme, l'artésunate constitue une alternative extrêmement rentable et abordable par rapport à la quinine. Les implications budgétaires liées à l'adoption de l'artésunate pour une utilisation habituelle lors des soins hospitaliers sont négligeables.

Резюме

Соотношение «затраты – эффективность» при парантеральном применении артесуната для лечения детей с тяжелой формой малярии в странах Африки к югу от Сахары

Цель Исследовать соотношение «затраты – эффективность» при парентеральном применении артесуната для лечения тяжелой формы малярии у детей, а также оценить его потенциальное влияние на бюджет больницы.

Методы Затраты на оказание стационарной медицинской помощи детям с тяжелой формой малярии оценивалось в четырех из 11 медицинских учреждений, включенных в «Сравнительное исследование эффективности применения хинина и артесуната при лечении малярии в странах Африки», которое охватывало свыше 5400 детей. Для расчета стоимости стационарной помощи фиксировались расход лекарств, лабораторные анализы и расход жидкостей для внутривенного введения по 2300 пациентам за период от назначения до отмены, а также продолжительность пребывания в стационаре. Данные увязывались с совокупными клиническими исходами и вводились в модель принятия решений для расчета затрат на один предотвращенный DALY и на один предотвращенный смертельный исход.

Результаты Средняя стоимость лечения больных с тяжелой формой малярии была аналогичной в обеих испытуемых группах: 63,5 долл. США (95% доверительный интервал, ДИ: 61,7–65,2) в группе хинина, и 66,5 долл. США (95% ДИ: 63,7–69,2) в группе артесуната. У детей, которых лечили артесунатом, смертность была на 22,5% ниже, чем у тех, кого лечили хинином, и отмечался тот же, чем у них, показатель неврологических осложнений: (группа артесуната: 2,3 DALY на 1 больного; группа хинина: 3,0 DALY на 1 больного). По сравнению с хинином как базовым уровнем, при лечении артесунатомпредельные затраты на 1 предотвращенный DALY и на 1 предотвращенный смертельный исход составляли 3,8 долл. США и 123 долл. США, соответственно.

Вывод Артесунат является высокоэффективным с точки зрения затрат и экономически доступным альтернативным лекарственным средством при лечении детей с тяжелой формой малярии. Бюджетные последствия применения артесуната для рутинного использования при оказании медицинской помощи в условиях больницы крайне незначительны.

Resumen

Relación coste-eficacia del artesunato para el tratamiento de niños con malaria grave en el África subsahariana

Objetivo Analizar la relación coste-eficacia del artesunato parenteral en el tratamiento de la malaria grave infantil y su posible impacto en los presupuestos hospitalarios.

Métodos En cuatro de los 11 centros incluidos en el Estudio comparativo de los tratamientos de la malaria con artesunato y quinina en África participaron más de 5400 niños. Para calcular el coste de la hospitalización se registraron los fármacos, las pruebas clínicas y los líquidos endovenosos suministrados a 2300 pacientes, desde su ingreso hasta el alta, según la duración del ingreso del paciente. Los datos se compararon con los resultados clínicos agrupados e

introducidos en un modelo de decisión para calcular el coste por año de vida ajustada por discapacidad (AVAD) evitada y el coste por muerte evitada.

Resultados El coste medio del tratamiento de los pacientes con malaria grave fue similar en los dos grupos del estudio: 63,5 dólares estadounidenses (US$) (intervalo de confianza del 95%, IC: 61,7–65,2) en el grupo de quinina y US$ 66,5 (IC del 95%: 63,7–69,2) en el grupo de artesunato. Los niños tratados con artesunato presentaron una mortalidad un 22,5% inferior que los tratados con quinina y la misma tasa de secuelas neurológicas: (grupo de

artesunato: 2,3 AVAD por paciente; grupo de quinina: 3,0 AVAD por paciente). En comparación con la quinina como referencia, el artesunato ha mostrado un coste incremental por AVAD evitado y un coste incremental por muerte evitada de US$ 3,8 y US$ 123, respectivamente.

Conclusión El artesunato es una alternativa a la quinina muy rentable y con una excelente relación coste-eficacia para el tratamiento de niños con malaria grave. Las implicaciones presupuestarias de la adopción del artesunato para su uso sistemático en la asistencia hospitalaria son insignificantes.

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