Cost-effectiveness of zinc as adjunct therapy for acute childhood diarrhoea in developing countries

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Objective To analyse the incremental costs, effects and cost-effectiveness of zinc used as adjunct therapy to standard treatment of acute childhood diarrhoea, including dysentery, and to reassess the cost-effectiveness of standard case management with oral rehydration salt (ORS).

Methods A decision tree was used to model expected clinical outcomes and expected costs under four alternative treatment strategies. The best available epidemiological, clinical and economic evidence was used in the calculations, and the United Republic of Tanzania was the reference setting. Probabilistic cost-effectiveness analysis was performed using a Monte-Carlo simulation technique and the potential impacts of uncertainty in single parameters were explored in one-way sensitivity analyses.

Findings ORS was found to be less cost-effective than previously thought. The use of zinc as adjunct therapy significantly improved the cost-effectiveness of standard management of diarrhoea for dysenteric as well as non-dysenteric illness. The results were particularly sensitive to mortality rates in non-dysenteric diarrhoea, but the alternative interventions can be defined as highly cost-effective even in pessimistic scenarios.

Conclusion There is sufficient evidence to recommend the inclusion of zinc into standard case management of both dysenteric and non-dysenteric acute diarrhoea. A direct transfer of our findings from the United Republic of Tanzania to other settings is not justified, but there are no indications of large geographical differences in the efficacy of zinc. It is therefore plausible that our findings are also applicable to other developing countries.

Keywords Zinc/therapeutic use/administration and dosage; Diarrhea/drug therapy; Dysentery/drug therapy; Rehydration solutions/economics; Fluid therapy/economics; Costs and cost analysis; Cost of illness; Uncertainty; Sensitivity and specificity; Developing countries; United Republic of Tanzania (*source: MeSH, NLM*).

Mots clés Zinc/usage thérapeutique/administration et posologie; Diarrhée/chimiothérapie; Dysenterie/chimiothérapie; Solution réhydratation/économie; Traitement par apport liquidien/économie; Coût et analyse coût; Coût maladie; Incertitude; Sensibilité et spécificité (Epidémiologie); Pays en développement; République-Unie de Tanzanie (*source: MeSH, INSERM*).

Palabras clave Cinc/uso terapéutico/administración y dosificación; Diarrea/quimioterapia; Disentería/quimioterapia; Soluciones para rehidratación/economía; Fluidoterapia/economía; Costos y análisis de costo; Costo de la enfermedad; Incertidumbre; Sensibilidad y especificidad; Países en desarrollo; República Unida de Tanzanía (*fuente: DeCS, BIREME*).

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Introduction

Diarrhoeal diseases are the cause of almost three million deaths annually (*1–3*), mainly among children less than 5 years of age. This represents a loss of nearly 100 million disability-adjusted life years (DALYs) (*3*). The majority of cases of diarrhoea and deaths from diarrhoea occur in children aged less than 5 years in the poorest regions of the world. About 35% of the deaths are attributable to acute non-dysenteric diarrhoea and an estimated 45% occur in children with persistent diarrhoea (*4*), which inflicts on the children a dangerous nutritional insult. Therapy using oral rehydration salt ORS and dietary management are therefore key components in the management of childhood diarrhoea (*5, 6*). For the treatment of dysentery, which is responsible for the remaining 20% of the deaths from diarrhoea (*4*), antimicrobials are indicated (*5, 6*). Although these measures are available for many of the world's children, diarrhoea continues to be a major cause of death and illness during childhood in developing countries.

Recent evidence has demonstrated that zinc supplementation has a considerable beneficial effect on the clinical course of acute diarrhoea (*7*). The use of zinc as an adjunct to standard case management of diarrhoea may therefore contribute substantially towards reducing the burden of diarrhoeal disease

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(*7–10*). The question of whether zinc should be administered to all children with acute diarrhoea, or only to those who do not present with dysentery, remains to be answered.

The objectives of this study were to analyse the incremental costs, effects and cost-effectiveness of zinc used as adjunct therapy to standard treatment of acute childhood diarrhoea. We also reassessed the cost-effectiveness of standard case management with ORS. This generalization facilitates the comparison with no diarrhoea management (the null-intervention), which, in turn, enables comparison with a broader set of health interventions competing for scarce resources.

Description of interventions

Three alternative treatment protocols were analysed:

I. current standard treatment with ORS;
II. zinc as adjunct therapy to current standard treatment for children with non-dysenteric diarrhoea; and
III. zinc as adjunct therapy to current standard treatment for all children with acute diarrhoea, including those with dysentery.

The standard care comparator of ORS is described in detail elsewhere (*5*). In general, it is recommended that ORS be given at home to children with diarrhoea and mild dehydration, and administered at a clinic if the dehydration is more pronounced (*5*). Zinc is most conveniently administered as dispersible tablets that can also be chewed or swallowed. Alternatively, zinc may be mixed with ORS (but this can make it difficult to obtain the correct dosage) (*11*), or dissolved in a syrup (which is more expensive than dispersible tablets). We therefore based our analysis on the use of dispersible tablets.

A likely protocol will advise 14 days of treatment with a daily dose of 10 mg elemental zinc for infants and 20 mg per day for older children (*7*). Whether zinc will also be recommended for children with dysentery is unclear because all but one of the efficacy trials conducted so far (*10*) have restricted the inclusion of study subjects to children with non-dysenteric diarrhoea. Zinc is likely to be as effective for treating those patients with dysentery who do not receive suitable antibiotic therapy as it is for treating patients with acute non-dysenteric diarrhoea. We assumed that zinc has no additional benefit for those patients with dysentery who do receive adequate antibiotic therapy.

Treating acute diarrhoea with zinc does not require additional assessment of the child (*10*). Zinc tablets can easily be added to the current treatment guidelines. Zinc is non-toxic, can safely be provided over the counter without a prescription, and can be offered where ORS is available, for example, at basic health posts, pharmacies and grocery shops. Zinc seems to be equally effective whether administered by carers or by field workers (*10*).

Methods

We performed a generalized incremental cost-effectiveness analysis using DALYs as the outcome measure to simplify the comparison of cost-effectiveness across disease groups and settings (*3*). Because the measured morbidity of diarrhoea is negligible compared to its measured mortality, calculations are also presented in terms of the number of child deaths averted. In the calculation of DALYs, we used a Tanzanian life table with a life expectancy of 46.5 years at birth (*12*). The costs per child death averted were also calculated. All monetary values are presented in 2001 US dollars (US$) and costs and health consequences are discounted using a rate of 3% as baseline. The costs and consequences were all calculated using hypothetical diarrhoea cases as the denominator.

We present direct costs and effects in a societal perspective, meaning that costs to the health system and some patient costs were included. To account for simultaneous uncertainties in both cost and effect measures, we used a stochastic Monte-Carlo simulation approach (*13*, *14*). Incremental and average costs, effects and cost-effectiveness were calculated for each of the alternative treatment protocols. Finally, a one-way sensitivity analysis was performed for key variables (*13*, *14*).

Mortality from diarrhoea

A consensus on case–fatality ratios (CFRs) for dysenteric and non-dysenteric diarrhoea has yet to be reached. The reported CFRs for acute non-dysenteric diarrhoea vary from 0.1% to 0. 6% (*15–17*); those for dysentery vary from 4% to 30% (*15*, *18–21*). The clinical and epidemiological settings in which these estimations were made were highly variable, making comparisons difficult. As most of the studies were hospital-based, and therefore presumably included mainly the most severely ill patients, it was assumed that most of these estimates of mortality from diarrhoea are higher than those in the corresponding communities.

We computed a mean CFR of 0.15% for diarrhoea in children aged less than 5 years from a median of 3.2 episodes per child per year and a yearly mortality rate from diarrhoea of 4.9 children per 1000 as reported in a recent meta-analysis (*22*). This meta-analysis probably represents the best current evidence on mortality from diarrhoea. For the purposes of this study, we calculated CFRs based on global estimates of the total annual incidence of diarrhoea (1.8 billion cases) and deaths (2.9 million) (*1*) and on published information about the distribution of diarrhoea-related deaths (*4*).

We searched using MEDLINE for English-language sources using the following keywords: children, dysentery, diarrhoea and persistent diarrhoea, and found a number of relevant publications. On the basis of weighted averages of the figures presented in these publications, we assumed that 7.5% of cases of acute diarrhoea are dysenteric (*10*, *23–27*) and that 5% become persistent (*10*, *15*, *26*, *28–34*). We assumed untreated dysentery to be four times more likely to result in death than dysentery appropriately treated with antibiotics, and that one third of the cases are treated adequately with antibiotics (*35*). The resulting estimates are reported in Table 1, and correspond well with the findings of the above-mentioned meta-analysis (*22*). Table 1 also includes the minimum and maximum values used in the probabilistic cost-effectiveness analysis in assumed triangular and asymmetric distributions. Minimum values were calculated as most likely values divided by 1.5 and maximum values were calculated as most likely values multiplied by 1.5.

Calculating effectiveness

The expected clinical outcomes for the three alternative interventions were calculated using a decision tree model (Fig. 1) (*36*). In the model, each of the alternative treatment protocols (I–III) is represented with a branch. A fourth branch was included for the no-treatment alternative in order to generalize the outcomes. For each branch, we allowed for the possibility that the acute diarrhoea either is or is not dysenteric. For dysentery, there is a possibility that patients have access to and adhere to adequate antibiotic treatment, and there is a possibility that they do not. Similarly, for patients receiving zinc or ORS, there is

a possibility that they adhere to the treatment guidelines and there is a possibility that they do not. An overview of the key assumptions is given in Table 2, and an overview of the assumed effectiveness (relative risks) of zinc in various settings is given in Table 1. Minimum values were calculated as most likely values divided by 1.5 and maximum values were calculated as most likely values multiplied by 1.5. For all end-points, patients either survive or die, depending on the CFRs and relative risks applicable to the alternative scenarios.

The morbidity component of the DALYs was calculated assuming an average age for the affected children of 1.5 years. We further assumed a mean duration of an episode of diarrhoea of 7 days (*16*, *17*), and a relative hazard for mean episode duration of 0.83 for patients receiving zinc. This is the weighted mean of relative hazards from seven different studies (*7*), and implies that the mean duration is reduced to 5.8 days in patients receiving zinc. A disability weight for diarrhoea of 0.119 was used (*3*).

Calculating costs

For standard case management, costs were calculated as the mean cost of diarrhoea management at four different dispensaries in the United Republic of Tanzania (*37*). The cost items included staff, drugs and medical supplies, utilities, stationery, uniforms and linen, cleaning, maintenance, travel, and annual costs of buildings, equipment, furniture and transportation (*37*). The discount rate of 10% for capital costs used in the study in Dar es Salaam (*37*) was reduced to 3% in the present study.

The above costs represent the current standard treatment of acute diarrhoea. This means that the costs of ORS and antibiotics are included. Assuming that there is treatment capacity available at the dispensaries, the incremental cost of providing zinc is limited to the cost of the zinc tablets. As market prices are not available for dispersible zinc tablets, their cost was based on a price offered to WHO (*38*) and calculated as shown in Table 3, assuming that tablets would be provided through the private sector (R.R. Madabida, personal communication, 2002). An overview of the facility and drug costs is given in Table 3. It was assumed that 25% of children requiring treatment would be infants who needed a dosage of 10 mg zinc per day for 14 days, and that the remaining 75% of the children would be older and would require 20 mg zinc per day for 14 days.

The uncertainty calculations were made using triangular distributions with the minimum and maximum values as most likely values ± 33%, respectively, for the drug costs. It should be noted that this formula is different from that used for risks and effects, because drug costs have a symmetrical scale unlike relative risks that are inherently non-symmetrical in scale. For facility costs, we used the lowest and highest values from the sites in the Tanzanian costing study (*37*) as minimum and maximum values. We used the decision tree (Fig. 1) to calculate the expected costs related to each intervention.

Uncertainty and sensitivity analysis

There is uncertainty attached to the various estimates of effectiveness and costs. The uncertainty analysis (Monte-Carlo simulation) is based on most likely, minimum, and maximum values in triangular distributions as shown in Table 1, Table 2 and Table 3. In the simulation, 3000 random draws from the triangular distributions were made and cost–effectiveness ratios (CERs) were calculated for each iteration. From these 3000 CERs, mean CERs with 95% confidence intervals were calculated for each of the alternative treatments (*39*). The confidence

Table 1. **Estimates of case–fatality ratios in acute diarrhoea and effectiveness of zinc, including most likely values and minimum and maximum likely values[a] used in the Monte-Carlo simulations**

Patients with acute diarrhoea	Case–fatality ratio				Relative risk when providing zinc as adjunct therapy			
	Most likely value (%)	Source ref.	Min. value (%)	Max. value (%)	Most likely value	Source ref.	Min. value	Max. value
Dysentery (bloody stools)								
Without adequate antibiotic treatment	0.58	(*1*), own[b]	0.39	0.87	0.50	Own[b]	0.33	0.75
With antibiotic treatment	0.14	(*1*), own[b]	0.10	0.22	1.00	Own[b]	0.67	1.00
Untreated non-dysenteric diarrhoea	0.18	(*1*), own[b]	0.12	0.27	0.50	(*8*)	0.33	0.75

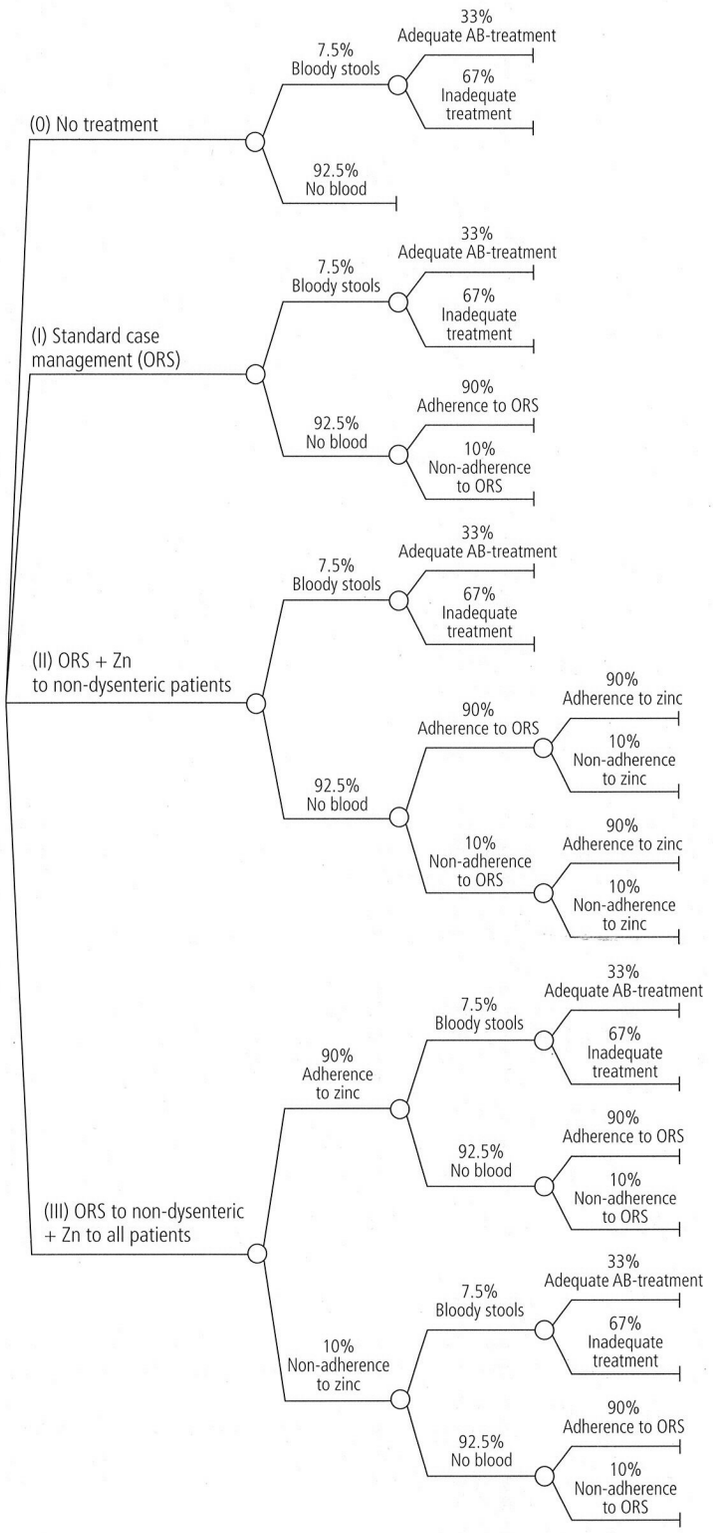
[a] Minimum values were calculated as most likely values divided by 1.5 and maximum values as most likely values multiplied by 1.5. Distributions were assumed to be triangular for all parameters.
[b] Own data; see text for details.

Table 2. **Key assumptions used to model the clinical outcomes of the three treatment protocols[a]**

	Most likely value (%)	Source ref.	Min. value (%)	Max. value (%)
% of all patients with acute diarrhoea who have dysentery	7.5	Own[b]	5	11
% of patients with dysentery receiving adequate antibiotic treatment	33	(*36*)	22	50
% of patients adhering to treatment with zinc and ORS	90	Own[b]	60	100
Effectiveness of treatment with ORS (relative risk)	0.5	(*18*)	0.33	0.75

[a] Most likely values and minimum and maximum likely values used in Monte-Carlo simulations are calculated as most likely values divided by 1.5 and most likely values multiplied by 1.5, respectively. Distributions are assumed to be triangular for all parameters.
[b] Own data; see text.

Fig. 1. **The decision tree used to model the expected survival rates for the null intervention (no treatment) and the three treatment alternatives, with baseline probabilities.** For each end-point, patients either die or survive depending on the probabilities reported in Table 1 and Table 2. An identical tree structure was used to model the expected costs of the treatment alternatives (ORS = oral rehydration salts; Zn = zinc; AB = antibiotic)



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intervals, which are direct outputs from the Monte-Carlo simulations, give a good impression of the precision of the estimates.

Uncertainty may also be attached to variables carrying value judgements. The impact of this uncertainty was determined in one-way sensitivity analyses (*40*). For the discount rate, a range of 0% to 5% was applied, with 3% as the baseline, while the age–weight modelling factor was varied from 1 (baseline) to 0 (no age-weighting). Because of the uncertainty attached to the

Table 3. **The unit costs for case management of acute diarrhoea and the incremental unit costs of providing zinc (in 2001 US$)**[a]

Facility costs for standard case management	Most likely value	Min.	Max.	Source
Recurrent costs	1.70	0.43	2.90	(*37*), own[b]
Capital costs	0.22	0.13	0.62	(*37*), own[b]
Total facility costs	**1.92**			
Incremental costs per treatment of providing zinc (recurrent costs only)				
Import price	0.0100			(*38*)
Insurance (1%) and freight (5%)	0.0006			(pers. comm.)[c]
Clearing cost (12.5%)	0.0013			(pers. comm.)[c]
Provision to wholesaler (30%)	0.0036			(pers. comm.)[c]
Provision to retailer (25%)	0.0039			(pers. comm.)[c]
Total incremental cost per tablet	**0.0194**			
Average no. of tablets per treatment	24.5			(*7*), own[b]
Total incremental costs per treatment	**0.47**	**0.33**	**0.62**	

[a] Triangular distribution is assumed for all cost variables. Minimum and maximum values for facility costs are taken from the costing study. Minimum and maximum values for incremental treatment costs are calculated as most likely value ± 33%.
[b] Own data; see text.
[c] Madabida RR, personal communication, 2002.

CFRs, one-way sensitivity analyses of these parameters were also made. For the CFR of dysentery with and without adequate treatment, the baseline divided and the baseline multiplied by 1.5 was used as the range. For the CFR of untreated non-dysenteric diarrhoea, 0.12% (baseline divided by 1.5) was used as the minimum value, and a CFR of 0.50% was used as the maximum value. This maximum value is considerably higher than the baseline times 1.5 (0.27%, used in Monte-Carlo simulation), and was used to enable inclusion of the value used in previous cost-effectiveness analyses (*17*). Finally, the effect of life expectancy at birth was analysed using a range from 37.9 years (Malawi males) as minimum to 83.9 years (Japanese females) as maximum values (*12*). These reflect the lowest and highest life expectancies worldwide.

Results

The reassessed mean CER for ORS (I) was US$ 113 per DALY averted, or about US$ 3200 per child death averted. The mean incremental CER of adding zinc to the treatment of patients without dysentery (I–II) was US$ 40 per DALY averted and roughly US$ 1200 per death averted. Expanding the programme to cover not only the non-dysenteric but also dysenteric cases of acute diarrhoea (II–III) yielded mean incremental CERs of US$ 11 per DALY and US$ 307 per death averted. The average mean CERs of providing ORS and zinc to all children with acute diarrhoea (III) was US$ 73 per DALY and about US$ 2100 per death averted. The mean CERs and their 95% confidence limits are given in Table 4. The confidence limits illustrate the cost-effectiveness in both pessimistic and optimistic scenarios.

The mean costs and DALYs from the Monte-Carlo simulations are presented separately in Fig. 2. The figure indicates that the slope of lines connecting the alternative interventions decreases when the interventions are sorted according to increasing effectiveness. We are therefore facing a situation with decreasing incremental CERs, which expresses extended dominance. The optimal treatment would therefore be the provision of zinc in addition to ORS to all patients (III), irrespective of budget constraints. However, as illustrated in Table 4, the confidence limits are so wide that extended dominance is not certain.

Sensitivity analyses

The sensitivity analyses revealed that the average CER for full introduction of zinc (III) was highly sensitive to the CFR in non-dysenteric diarrhoea. Similar observations were made for standard case-management (I) and the incremental CER of moving from intervention I to intervention II. The results were also found to be sensitive to the discount rate. The effects of life expectancy and age-weighting were of less importance, but CFR in dysentery was important for the incremental CER from II to III. These findings are illustrated in Table 5.

Discussion

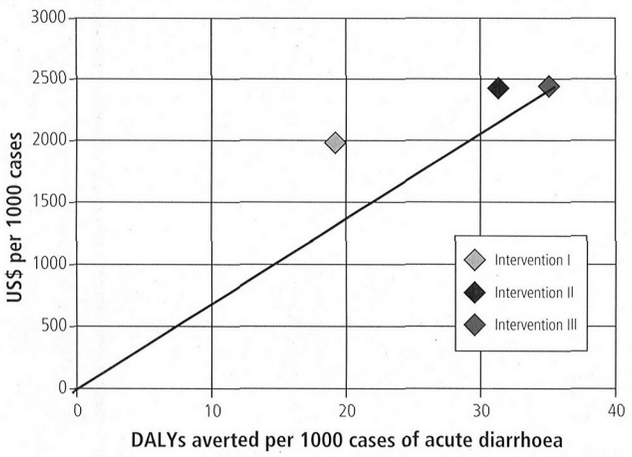
Two main conclusions can be drawn from these findings. Firstly, that ORS costs more than four times as much per DALY averted

Table 4. **Cost–effectiveness ratio (CER) point estimates and 95% confidence limits for management of acute diarrhoea in children**[a]

	US$ per DALY averted		US$ per child death averted	
Average CER (I)	113	(25–201)	3213	(721–5705)
Incremental CER (I–II)	40	(13–66)	1176	(375–1978)
Incremental CER (II–III)	11	(3–18)	307	(93–521)
Average CER (III)	73	(32–114)	2098	(945–3251)

[a] The management strategies are as follows: standard case management ORS (I); zinc as adjunct therapy to patients without dysentery (I–II); further expansion of the programme to treat all cases of acute diarrhoea (II–III); the full programme (III). The figures are from the Monte-Carlo simulations and illustrate the level of uncertainty in the analyses. The confidence limits indicate the cost-effectiveness in scenarios that are very pessimistic and very optimistic.

Fig. 2. **Mean total costs and disability-adjusted life years (DALYs) averted per 1000 acute diarrhoea episodes[a] (ORS = oral rehydration salts)**



[a]Treatment (I) ORS to all eligible children with diarrhoea; (II) ORS to all + zinc to non-dysenteric patients only; (III) ORS + zinc to all children with diarrhoea. The extra cost of providing zinc to the approximately 7.5% of children with dysenteric diarrhoea is small, while the expected health effect is relatively large. The best value for money (lowest cost–effectiveness ratio) is therefore probably achieved if zinc is provided as adjunct to standard case management to all children with acute diarrhoea, including those with dysentery.

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than previously reported (*17*). This difference is primarily due to the difference in assumptions about the CFR in acute non-dysenteric diarrhoea that are described in the Methods section. The present study did not find that the available evidence supported the assumptions previously made about mortality. Our results on cost-effectiveness for ORS are more in line with recent estimates made by the WHO-CHOICE project (*41*). As they cost less than the Tanzanian GDP per capita of US$ 270 (*42*) per DALY averted, all interventions explored in this study may be regarded as highly cost-effective (*43*). This is true even when a pessimistic scenario is applied (i.e. upper confidence limits).

Secondly, the mean CER was found to be reduced by more than one-third from US$ 113 for ORS alone (I) to US$ 73 per DALY averted when ORS was combined with zinc for treatment of all children with acute diarrhoea (III). Indications of extended dominance suggest that alternatives I and II should be excluded from consideration (*14*), but the level of uncertainty necessitates that this conclusion is moderated accordingly. If, for example, the coverage rate for appropriate antibiotic treatment is higher than assumed here, and if the conservative assumption that zinc has no incremental benefit in such cases is correct, dominance of intervention III over intervention II would no longer be the situation. The decision as to whether or not to change from alternative II to alternative III in such a situation would depend on available health budgets. Most probably, however, the most cost-effective management of diarrhoea would be achieved by moving directly to the full implementation of the zinc programme (III).

Our analyses are based on the assumption that the zinc treatment is perfectly divisible, and that there are constant returns to scale; in other words that it is possible to deliver the treatment in smaller or larger numbers without affecting the CERs (*14*). Furthermore, this study considered the direct costs and effects of zinc, but not the indirect costs and effects. For example, the drug substitution effect of zinc was not modelled. It has been shown that the use of un-indicated antibiotics, for example antibiotics used in non-dysenteric diarrhoea, is significantly less frequent in areas where zinc is used in addition to ORS, than in areas where only ORS is used (*7, 8, 44*). Also, the use of remedies that have undocumented effects on acute diarrhoea, such as herbal medicines and treatment given by traditional healers was significantly lower in the areas supplied with zinc (R. Black, personal communication, 2003) (*8*). The indirect effect of zinc on stunting, which could potentially increase the weight of the morbidity component in the calculations, is another parameter that was not modelled.

There are no indications of large geographical differences in the efficacy of zinc (*7, 9*). It is thus plausible that zinc therapy has a similar potential benefit in African, Asian and Latin American countries. We believe our results would be useful to policy-makers in many developing countries, but we do not recommend a direct transfer of conclusions from our Tanzanian study to other settings. Because of different cost levels in different settings, cost-effectiveness is likely to vary more than effectiveness between settings.

Although we have used substantially lower CFRs for diarrhoea than have been used in previous studies, there is still a

Table 5. **Influence of changes in key input variables on average and incremental cost–effectiveness ratios (CERs) (in US$ per DALY averted)[a]**

Input variable	Input value		Average CER (I)[b]		Incremental CER (I–II)[b]		Incremental CER (II–III)[b]		Average CER (III)[b]	
	Low	High	Low	High	Low	High	Low	High	Low	High
CFR[c] untreated diarrhoea without dysentery	0.12%	0.50%	137	32	56	13	NA	NA	93	25
Discount rate	0%	5%	45	136	19	55	5	14	33	97
Life expectancy at onset of disability	37.10	83.90	104	80	43	33	11	8	75	57
CFR[c] of dysentery without adequate treatment	0.39%	0.87%	NA	NA	NA	NA	14	6	68	62
Age-weighting	0 = no	1 = yes	103	91	37	37	10	9	70	66

[a] The sensitivity analyses are based on base-case calculations, and not output from the Monte-Carlo simulations.
[b] The management strategies are as follows: standard case management/ORS (I); zinc as adjunct therapy to patients without dysentery (I–II); further expansion of the programme to treat all cases of acute diarrhoea (II–III); the full programme (III).
[c] CFR = case fatality rate.

possibility that our estimates need further adjustment. During the last couple of decades, there has been a trend towards a decrease in the numbers of deaths from diarrhoea worldwide (*1*, *2*, *45*). Our model suggests that a further reduction in mortality from diarrhoea would translate into reduced CFRs, consequently making diarrhoea management less cost-effective.

One question that would need to be addressed is how a programme for treatment with zinc should be financed. If patients have to pay for the zinc tablets themselves, the treatment, from the point of view of the government, would have minimal implications either in financial terms, or in terms of how many patients could be treated. However, although US$ 0.25 for a full treatment course for an infant might seem a negligible cost, in extremely resource-poor settings this cost may still result in lack of access to the treatment for some poorer patients. If the zinc treatment were to be financed from a fixed health budget, either: (a) fewer diarrhoea patients could be offered treatment, or (b) fewer resources would be available for treating other health conditions. Because full implementation of the zinc programme (III) seems to dominate both the alternatives (I and II), the total performance of the health system would, according to our analysis, be improved if (a) is the case. This is because averting one DALY or one child death would cost less using intervention III than using the alternatives. In case (b), total performance of the health system depends on the cost-effectiveness of treatments being substituted by zinc therapy. (For example, if a health authority stopped treating tuberculosis patients, which has been demonstrated to be extremely cost-effective, in order to finance zinc treatment of diarrhoea, overall health system performance is likely to decrease.)

We have demonstrated that zinc used as adjunct therapy to standard case management of acute diarrhoea represents good value for money. Moreover, diarrhoeal diseases are overrepresented in one of the most vulnerable population groups, namely, children less than 5 years of age from the poorest segments of the population in developing countries. Although we have not made a formal distribution analysis, this suggests that zinc therapy represents an equitable resource allocation as well as an efficient one. We therefore believe that there is good evidence to advise that zinc be included into the standard case management of both dysenteric and non-dysenteric acute diarrhoea. ■

Conflicts of interest: none declared.

Résumé

Rapport coût-efficacité de l'administration de zinc comme traitement d'appoint de la diarrhée aiguë de l'enfant dans les pays en développement

Objectif Analyser le coût différentiel, l'effet et le rapport coût-efficacité de l'administration de zinc comme appoint au traitement standard de la diarrhée aiguë de l'enfant, dysenterie comprise, et réévaluer le rapport coût-efficacité de la prise en charge standard des cas par les sels de réhydratation orale (SRO).

Méthodes On a utilisé un arbre de décision pour modéliser l'issue clinique et les coûts prévus, en envisageant quatre alternatives de traitement. Les calculs ont été effectués à partir des meilleures données épidémiologiques, cliniques et économiques disponibles, et la République-Unie de Tanzanie a été choisie comme site de référence. Une analyse probabiliste du rapport coût-efficacité a été faite selon la méthode de simulation de Monte-Carlo et l'impact potentiel de l'incertitude sur les divers paramètres a été exploré au moyen d'analyses de sensibilité unilatérales.

Résultats Les sels de réhydratation orale avaient un moins bon rapport coût-efficacité qu'on ne le pensait. L'utilisation de zinc comme traitement d'appoint améliorait de façon significative le coût-efficacité de la prise en charge standard des cas de diarrhée, dysentériques ou non. Les résultats étaient particulièrement sensibles aux taux de mortalité dans la diarrhée non dysentérique, mais les diverses alternatives étaient d'un très bon rapport coût-efficacité même pour les scénarios pessimistes.

Conclusion On dispose de suffisamment d'éléments pour recommander d'inclure le zinc dans la prise en charge standard des cas de diarrhée aiguë dysentérique ou non. S'il n'est pas justifié de transposer directement nos résultats de République-Unie de Tanzanie dans d'autres contextes, rien n'indique que l'efficacité du zinc subisse d'importantes variations géographiques. Il est par conséquent plausible que nos résultats puissent s'appliquer à d'autres pays en développement.

Resumen

Costoeficacia del zinc como terapia auxiliar de la diarrea infantil aguda en los países en desarrollo

Objetivo Analizar el costo marginal, los efectos y la costoeficacia del zinc usado como terapia auxiliar del tratamiento estándar de la diarrea infantil aguda, incluida la disentería, y reevaluar la costoeficacia del tratamiento estándar de los casos con sales de rehidratación oral (SRO).

Métodos Se empleó un arbol decisional para modelizar los resultados clínicos esperados y los costos esperados bajo cuatro estrategias terapéuticas alternativas. Los cálculos se basaron en la mejor evidencia epidemiológica, clínica y económica disponible, y como entorno de referencia se eligió la República Unida de Tanzanía. El análisis probabilístico de la costoeficacia se llevó a cabo mediante un método de simulación de Monte Carlo, y para examinar la posible repercusión de la incertidumbre en parámetros individuales se realizaron análisis unidireccionales de la sensibilidad.

Resultados Se observó que las SRO eran menos costoeficaces de lo que se creía. El uso del zinc como terapia auxiliar mejoró significativamente la costoeficacia del tratamiento estándar de la diarrea tanto en los casos de disentería como en los otros casos. Los resultados dependieron muy estrechamente de las tasas de mortalidad en el caso de la diarrea no disentérica, pero las intervenciones alternativas pueden considerarse sumamente económicas aun en los escenarios pesimistas.

Conclusión La evidencia disponible autoriza a recomendar la inclusión del zinc en el tratamiento estándar de los casos de diarrea tanto disentérica como no disentérica. No estaría justificado trasladar directamente nuestros resultados de la República Unida de Tanzanía a otros entornos, pero no hay ninguna razón para pensar que existan grandes diferencias geográficas en cuanto a la eficacia del zinc. Cabe pensar, por tanto, que nuestros resultados son también aplicables a otros países en desarrollo.

ملخص

مردودية إعطاء الزنك كعلاج مساعد للإسهال الحاد بين الأطفال في البلدان النامية

الغرض: تحليل التكاليف الإضافية، والتأثيرات، والمردودية للزنك المستخدم كعلاج مكمل للمعالجة المعيارية للإسهال الحاد بين الأطفال، بما في ذلك الزحار، وإعادة تقييم فعالية المعالجة المعيارية للحالات عن طريق ملح الإمهاء الفموي.

الطريقة: تم استخدام شجرة قرارات لوضع النموذج المتوقع للنتائج السريرية والتكاليف المتوقعَّة من تنفيذ أربع استراتيجيات بديلة للمعالجة. وتم استخدام أفضل البيِّنات الإبيدميولوجية (الوبائية) والسريرية والاقتصادية المتاحة في الحسابات، وكانت جمهورية تنزانيا هي الموقع المرجعي. وتم إجراء تحليل احتمالي للمردودية باستخدام طريقة مونت كارلو للمحاكاة، مع استطلاع الآثار الممكنة للايقين في المثابتات الفردية من خلال تحاليل أحادية الاتجاه للحساسية.

الموجودات: تبيَّن أن ملح الإمهاء الفموي أقل مردودية مما كان يُظن. ولوحظ أن إعطاء الزنك كعلاج مساعد قد أدى إلى تحسين ملموس لفعالية المعالجة المعيارية للإسهال الناجم عن الزحار أو غيره من الأمراض. وكانت النتائج حساسة بشكل خاص لمعدلات الوفيات الناجمة عن الإسهال غير المتسبِّب عن الزحار، ولكن يمكن وصف التدخُّلات البديلة بأنها عالية المردودية حتى في السيناريوهات التشاؤمية.

الحصيلة: توجد بيِّنات كافية تسوِّغ التوصية باستخدام الزنك ضمن المعالجة المعيارية لحالات الإسهال الحاد الناجمة عن الزحار أو غيره من الأمراض. ولا يوجد مبرِّر للتحويل المباشر لنتائج هذه الدراسة من جمهورية تنزانيا إلى مواقع أخرى، ومع ذلك لا توجد مؤشرات على اختلافات جغرافية كبيرة في كفاءة الزنك. ولذلك يمكن القول إن نتائج هذه الدراسة يمكن تطبيقها على بلدان نامية أخرى.

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