Seasonal malaria chemoprevention in the Sahel subregion of Africa: a cost-effectiveness and cost-savings analysis

Colin Gilmartin, Justice Nonvignon*, Matthew Cairns, Paul Milligan, Fadima Bocoum, Peter Winskill, Diego Moroso, David Collins**

Summary

Background The intermittent administration of seasonal malaria chemoprevention (SMC) is recommended to prevent malaria among children aged 3–59 months in areas of the Sahel subregion in Africa. However, the cost-effectiveness and cost savings of SMC have not previously been evaluated in large-scale studies.

Methods We did a cost-effectiveness and cost-savings analysis of a large-scale, multi-country SMC campaign with sulfadoxine–pyrimethamine plus amodiaquine for children younger than 5 years in seven countries in the Sahel subregion (Burkina Faso, Chad, Guinea, Mali, Niger, Nigeria, and The Gambia) in 2016. The financial and economic costs were analysed from the programmatic perspective and are reported in 2016 US$ for each country. The estimated numbers of averted malaria cases, deaths, and disability-adjusted life-years (DALYs) were based on numbers of SMC treatments administered and modelled malaria transmission. Cost savings were calculated from a programmatic perspective corresponding to the diagnostic and treatment costs for malaria cases averted.

Findings The total cost of SMC for all seven countries was $22·8 million, and the weighted average economic cost of administering four monthly SMC cycles was $3·63 per child (ranging from $2·71 in Niger to $8·20 in The Gambia). Based on 80% modelled effectiveness of SMC, the incremental economic cost per malaria case averted ranged from $2·91 in Niger to $30·73 in The Gambia; the cost per severe case averted ranged from $119·63 in Niger to $506·00 in The Gambia; the cost per death averted ranged from $533·56 in Niger to $2256·92 in The Gambia; and the cost per DALY averted (discounted by 3%) ranged from $18·66 in Niger to $78·91 in The Gambia. The estimated total economic cost savings to the health systems in all seven countries were US$66·0 million and the total net economic cost savings were US$43·2 million.

Interpretation SMC is a low-cost and highly cost-effective intervention that contributes to substantial cost savings by reducing malaria diagnostic and treatment costs among children.

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*Contributed equally

Management Sciences for Health, Arlington, VA, USA (C Gilmartin MSc, D Collins MA); **University of Ghana School of Public Health, Accra, Ghana** (J Nonvignon PhD); **London School of Hygiene & Tropical Medicine, London, UK** (M Cairns PhD, Prof P Milligan PhD); **Institut de Recherche en Sciences de la Santé, Ouagadougou, Burkina Faso** (F Bocoum PhD); **MRC Centre of Global Infectious Disease Analysis, Imperial College London, London, UK** (P Winskill PhD); **Malaria Consortium Regional Office, Kampala, Uganda** (D Moroso MPH); **Boston University School of Public Health, Boston, MA, USA** (D Collins)

Correspondence to: Colin Gilmartin, Management Sciences for Health, Arlington, VA 22203, USA
cgilmartin@msh.org

Introduction

In sub-Saharan Africa, almost 70% (292 000 of 429 000) of malaria deaths in 2015 occurred in children younger than 5 years.[1] In the Sahel, where the majority of childhood malarial disease and deaths occur during and immediately after the short rainy season, WHO recommends the intermittent administration of seasonal malaria chemoprevention (SMC) with sulfadoxine–pyrimethamine plus amodiaquine to prevent *Plasmodium falciparum* malaria among children aged 3–59 months.[2] The objective of SMC is to maintain therapeutic antimalarial medicine concentrations in the blood throughout the period of greatest malarial risk.[2] If given to populations at risk, SMC could avert several million malaria cases and tens of thousands of childhood deaths due to malaria annually.[3] Despite this evidence, as of 2015, SMC had been administered largely through small-scale (ie, subnational) or pilot projects, with ten countries adopting SMC as a national policy.[1]

Recognising the potential health impact of large-scale SMC distribution, in 2014, Unitaid launched the Achieving Catalytic Expansion of Seasonal Malaria Chemoprevention in the Sahel (ACCESS-SMC) project, which supported SMC administration in 2015 and 2016 in seven countries in the Sahel: Burkina Faso, Chad, Guinea, Mali, Niger, Nigeria, and The Gambia. ACCESS-SMC promoted the widespread adoption of SMC by showing its feasibility and impact on a large scale and creating the demand for, and the supply of, SMC medicine. In collaboration with National Malaria Control and Elimination Programs, ACCESS-SMC provided nearly 12·5 million monthly SMC cycles in 2015 and 25·1 million in 2016.

Although studies have shown the safety,[4] potential effectiveness,[3] and cost-effectiveness[5–7] of SMC using sulfadoxine–pyrimethamine plus amodiaquine, no cost-effectiveness studies of large-scale or multi-country programmes have been done, nor any cost-savings analyses of SMC. The aim of this study was to evaluate the cost-effectiveness of SMC in seven countries in the Sahel, in terms of its cost per averted malaria case, per averted severe malaria case, per averted death, and per averted

Research in context

Evidence before this study

We searched PubMed, Cochrane Library, Malaria in Pregnancy Library, African Journals Online, Cumulative Index to Nursing and Allied Health Literature, and Google Scholar for studies on seasonal malaria chemoprevention (SMC) and intermittent preventive treatment and their costs, cost-effectiveness, cost savings, and cost barriers. The search was limited to English language articles published from Jan 1, 2007, to May 31, 2017. The keywords "malaria OR falciparum" were combined with the following search terms: "economics", "cost", "cost sharing", "cost effectiveness", "cost allocation", "cost control", "cost of illness", "health care costs", "provider costs", "societal costs", "intermittent preventive treatment", "sulfadoxine", "sulphadoxine", and "pyrimethamine". Our search identified 20 studies, of which 15 reported costs associated with SMC or intermittent preventive treatment. Eight studies reported financial and economic costs; however, three did not present financial costs and four did not present economic costs. This previous research indicated that the administration of SMC to children in the Sahel subregion of Africa could avert millions of cases of *Plasmodium falciparum* malaria and thousands of deaths per year. However, to our knowledge, no studies have evaluated the cost-effectiveness or corresponding cost savings for large-scale distribution of SMC (ie, beyond small-scale subnational or pilot projects within countries in the region).

Added value of this study

This study provides timely and important evidence on the cost, cost-effectiveness, and potential cost savings of the first large-scale, multi-country SMC campaign. The study shows that SMC, when distributed on a large scale, is a cost-effective approach to reducing the burden of malaria in children younger than 5 years in the Sahel and can result in large cost savings when accounting for malaria cases averted.

Implications of all the available evidence

The findings of this study will help country health systems and technical and financial partners to evaluate and prioritise investments in malaria and advance global efforts for malaria control and prevention. The continued implementation and expansion of SMC in eligible areas in and outside of the Sahel subregion could help to reduce the burden of malaria, which remains one of the leading causes of morbidity and mortality among young children globally. By reducing malaria cases and deaths, as well as associated costs for diagnosis and treatment, SMC could also contribute to substantial cost savings incurred by national health systems.

disability-adjusted life-year (DALY). The cost savings due to SMC were also estimated from the programmatic perspective, related to the diagnosis and treatment costs that would have been incurred in the absence of SMC.

Methods

Study design

The analysis comprises two main components: a cost-effectiveness analysis of the incremental costs and effects of SMC from a programmatic perspective, and a cost-savings analysis to estimate the treatment and diagnostic costs saved based on malaria cases averted. The cost-effectiveness analysis component provides only a partial view of the intervention's benefits because it did not account for net savings. The reporting of results followed the Consolidated Health Economic Evaluation Reporting Standards checklist (appendix pp 3–6).

See Online for appendix

Intervention

This study was done after the SMC campaign (July to December, 2016) and the time horizon of the analysis was 1 year (2016). SMC was administered in once monthly cycles for 4 months, with the timing depending on the malaria transmission patterns in each country (table 1). Each monthly cycle lasted 3–5 days, depending on the expected number of children that SMC distributors could reach in their catchment areas (appendix pp 7–10).

Each cycle, the first sulfadoxine–pyrimethamine plus amodiaquine dose was provided to eligible children by trained distributors on day 1 and the remaining two doses of amodiaquine were provided by the children's caregivers on days 2 and 3. The method of SMC distribution was a mixture of door-to-door, fixed-point, and mobile-point distribution, depending on the country and context. In 2016, 47 238 trained distributors, comprising both unpaid volunteers and salaried health centre personnel, administered SMC.

The number of monthly SMC treatments given to children younger than 5 years was estimated from ACCESS-SMC distribution records, adjusted to account for some treatments given to older children. The percentage of treatments that were administered to children aged 5 years or older was estimated based on the population age structure in each country according to UN World Population Prospects projections[8] and estimates obtained from coverage surveys.[9] In total, 25·1 million monthly SMC cycles were administered, of which an estimated 21·9 million were given to children younger than 5 years (table 1).

Cost analysis

Using an ingredients-based approach, the study estimated the economic cost of the intervention in 2016, comprising the recurrent financial costs incurred (for non-governmental organisations [NGOs]

	Burkina Faso	Chad	Guinea	Mali	Niger	Nigeria	The Gambia
Programme overview							
Months of SMC distribution	July to October	August to December	July to October	July to October	August to October	August to November	July to October
Days per monthly SMC cycle	4	3	4	5	5	4	5
Geographical coverage	31 districts in six regions	14 districts in four regions	Eight districts in four regions	20 districts in five regions	11 districts in four regions	34 local government areas in two states	18 districts in two regions
Distribution approach	Door-to-door and fixed-point at health centres	Door-to-door	Door-to-door	Fixed-point and mobile-point	Door-to-door, fixed-point, and mobile-point	Door-to-door and fixed-point	Door-to-door
Number of distributors	13 957	8029	2234	5318	3809	13 309	582
SMC coverage							
Monthly SMC cycles administered (all ages)	5 780 062	2 511 371	1 750 224	4 667 224	3 810 088	6 301 058	297 453
Monthly SMC cycles administered (<5 years)*	4 479 548	2 297 904	1 473 689	4 125 826	3 470 990	5 746 565	290 314
SMC distributed per monthly cycle (all ages)							
Cycle 1	1 325 487	615 671	439 796	1 060 268	915 334	967 009†	74 666
Cycle 2	1 437 420	652 539	416 822	1 126 460	978 011	1 763 595	75 741
Cycle 3	1 488 996	712 192	449 513	1 197 464	969 810	1 765 074	73 955
Cycle 4	1 528 159	530 969†	444 093	1 283 032	946 933	1 805 380	73 091
Number of cycles of SMC received by children‡, %							
None	0·7%	8·5%	3·3%	8·6%	7·9%	17·3%	16·6%
One cycle	0·7%	24·0%	3·2%	5·0%	5·2%	19·2%	6·4%
Two cycles	2·3%	27·0%	11·0%	9·6%	14·4%	20·5%	11·6%
Three cycles	5·1%	28·1%	9·5%	19·9%	22·3%	23·4%	21·7%
Four cycles	91·2%	12·4%	73·0%	56·9%	50·2%	19·5%	43·7%
Monthly SMC cycles by distribution approach (all ages), n (%)							
Door to door	5 682 031 (98·3%)	2 511 371 (100%)	1 750 224 (100%)	0	207 023 (5·4%)	0	297 453 (100%)
Fixed point	98 031 (1·7%)	0	0	982 128 (21·0%)	0	0	0
Mobile point	0	0	0	3 685 096 (79·0%)	0	0	0
Mixed methods	0	0	0	0	3 603 065 (94·6%)	6 301 058 (100%)	0

SMC=seasonal malaria chemoprevention. *The percentage of SMC treatments going to children younger than 5 years was estimated based on data from the ACCESS-SMC coverage surveys and UN country-specific estimates of the percentage of children in each age group. †In Nigeria and Chad, SMC medicine shortages contributed to low coverage in the first cycle in Nigeria and the fourth cycle in Chad, and fewer children were reached compared with other cycles. ‡Coverage estimates are survey-weighted estimates from surveys in 13 063 children (874 in Burkina Faso, 1010 in Chad, 1743 in Guinea, 799 in Mali, 5646 in Niger, 1853 in Nigeria, and 1138 in The Gambia).

Table 1: **SMC programme overview and coverage in the Sahel subregion of Africa in 2016**

and governments) and the opportunity costs of labour by non-salaried volunteer distributors (appendix pp 11–14). The analyses were done using Microsoft Excel 2016. Costs were not discounted because they were incurred within the 1-year time horizon of the intervention.

Costs were calculated separately for each country and were a mixture of actual and normative costs. Programmatic data on the numbers and types of SMC distributors and supervisors were provided by in-country partners. Financial costs were obtained from accounting and budget records of implementing NGO partners and through interviews with personnel involved in programme management, supervision, and distribution. Normative data on the time spent by Ministry of Health (MOH) supervisors and managers were collected through interviews in each country. The costs of MOH labour were based on the average total time spent supporting the campaign multiplied by the average hourly wage (assuming 8 h of work per day), which was based on the average monthly gross income (from all sources, including salary). Per diem payments were considered a financial cost.

The opportunity cost of volunteer, non-salaried distributors was calculated based on interviews and considered the number of hours spent on distribution, training, and other activities during each monthly cycle. These costs were estimated by multiplying the total number of hours spent during the campaign by the income they would have received for other productive activities (based on the national daily average minimum wage in each country). Costs were estimated in 2016 US$. If local currency was used, costs were converted using 2016 exchange rates, with $1 equal to 591 XOF, 591 XAF, 8347 GNF, 260 NGN, or 43 GMD. Sources for currency rates and national average wages used for this analysis can be found in the appendix (pp 11–14).

Predicting malaria cases, deaths, and DALYs averted by SMC

Modelled predictions of malaria cases in the absence of SMC were estimated using a combination of methods. A mathematical model of malaria transmission estimated the incidence of malaria, severe malaria, and malaria deaths at the level of the first administrative subdivision in each country.[10] The administrative subdivisions were calibrated to estimates of the prevalence of *P falciparum* from the Malaria Atlas Project and incorporated expected effects of long-lasting insecticidal nets based on 2015 coverage. The predicted incidence was adjusted by a scale factor based on clinical trials in Burkina Faso and Mali in 2016,[9] with model predictions for the same locations. For Chad, Niger, and northwest Nigeria, available prevalence data were scarce and out of date; therefore, the analysis used adjusted estimates, relying on prevalence data obtained from surveys in ACCESS-SMC areas at the end of the 2015 transmission season, and assuming a linear relationship between incidence and prevalence. To capture uncertainty in the incidence, a range of plausible values was calculated (appendix pp 15–29). For the sensitivity analysis, we assumed that the uncertainty in the mean incidence in each country could be as much as half of the difference between the smallest and largest country estimate. Therefore, a range was obtained by calculating the central estimate for each country plus or minus a quarter of the overall range.

The number of malaria cases that would have occurred in the counterfactual scenario, in which children did not receive SMC, was estimated by multiplying the monthly malaria incidence by the number of children younger than 5 years who were treated in that month. Estimates of the number of malaria cases averted by SMC in each month were then obtained by multiplying the estimated total number of malaria cases in the counterfactual scenario by 0·20 or 0·15 (ie, assuming modelled effectiveness of 80% or 85% in the month SMC is administered, respectively, with no effect outside this time period). The effectiveness of SMC in the 28 days after treatment was estimated as 88% (95% CI 79–94) in a series of case-control studies.[11] The results presented in this analysis are for 80% SMC effectiveness and use lower-bound estimates of malaria incidence in each country, therefore representing a conservative estimate of SMC effectiveness. Additional details on the lower-bound and upper-bound estimates for 80% and 85% effectiveness are provided in the appendix (pp 15–29). The same logic and the same assumptions regarding malaria incidence and SMC effectiveness were used to estimate the severe malaria cases averted by SMC.

The number of deaths averted was estimated from the number of severe cases averted, assuming a constant case fatality rate among severe cases, and also scaling by a factor to account for the fact that not all severe cases present to a health facility. DALYs averted were derived as a product of the total estimated number of deaths averted and DALYs per death. The estimate of 28·6 discounted (at 3%) DALYs and 65·4 undiscounted DALYs per death (average age of 2 years) was derived from a randomised controlled trial on home management of fever among children in Ghana.[12] We also estimated DALYs without age weighting.

Cost-effectiveness analysis

SMC was considered an additional intervention to existing health interventions already being delivered in each country. Incremental cost-effectiveness ratios (ICERs) were calculated by dividing the total economic cost of the SMC intervention in each country by the corresponding effectiveness estimates for children younger than 5 years. ICERs are presented with and without discounting of DALYs. The cost per child treated with the recommended four monthly cycles of SMC was estimated by dividing the total economic cost by the equivalent number of children younger than 5 years who received four doses in each country. The equivalent number of children was calculated by dividing the total number of monthly cycles in the under-5 age group by four monthly cycles.

Cost-effectiveness thresholds, according to WHO-CHOICE standards,[13] were used to determine the cost-effectiveness of SMC relative to each country's 2016 gross domestic product (GDP) per capita (according to World Bank data). Based on this approach, an intervention (per DALY averted) that costs less than three-times the country's GDP per capita is considered cost-effective, and an intervention that costs less than the GDP per capita is considered highly cost-effective. We present the ICERs under two scenarios: scenario one includes effects in children younger than 5 years and total costs of the intervention (which include costs to older children, given that in reality some older children received SMC), and scenario two includes the apportioned costs and effects for only children younger than 5 years (appendix pp 29–32).

Cost-savings analysis

Cost savings of SMC were estimated from a programmatic perspective. Malaria diagnosis and treatment costs were based on a review by White and colleagues[14] of cost studies done in several countries in Asia and Africa and figures were inflated to 2016 US$ using the inflation rate of 11·0% for the years 2009 to 2016. Because these figures included costs from Asia and South Africa, which were generally higher than the costs in other sub-Saharan African countries, the analysis used only the first quartile medians for calculating cost savings and therefore may be conservative. The first quartile median economic diagnosis and treatment costs were $8·86 for uncomplicated malaria cases and $28·03 for severe malaria cases, with severe malaria treatment costs being incurred at the hospital inpatient level. These unit costs were then multiplied by the numbers of malaria cases and severe malaria cases averted in each country to estimate the

total costs saved. It was assumed that severe malaria cases would have been initially treated as uncomplicated cases before receiving recommended treatment. It was assumed that 60% of malaria cases in children younger than 5 years would be diagnosed and treated at a health facility.[15] Net economic savings were calculated by subtracting the cost of the intervention from the expected cost savings in each country.

Sensitivity analysis

One-way sensitivity analyses were done to test the robustness of the ICERs by varying key cost and effectiveness estimates that had some degree of uncertainty. These included using undiscounted and discounted (3%) DALYs, MOH management costs (–50% to +20%) and the monthly protective effectiveness of SMC (70% to 90%). MOH management costs were reduced by 50% in the low scenario, based on widespread consensus among the authors that these estimates were overstated by MOH officials, and increased by 20% in the high scenario. The sensitivity analysis also considered the effect of changes in the percentage of malaria cases in children younger than 5 years that would be diagnosed and treated at a health facility (30% to 70%; appendix pp 33–37).

Role of the funding source

The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. CG, JN, and DC had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

Among the seven countries, the total number of SMC doses administered ranged from 297 453 in The Gambia to 6·3 million in Nigeria. The majority of SMC doses administered reached the intended target population of children younger than 5 years. SMC administration methods varied among countries but the most common were door-to-door and mixed-method approaches. The total recurrent economic cost for all ages was $22·8 million, comprising $20·6 million in financial costs and $2·2 million in volunteer opportunity costs (table 2). SMC drugs and supplies represented the highest financial cost in every country, followed by the per diem and travel payments made to the distributors, except in The Gambia, where NGO programme management costs were the second-highest costs. The weighted average economic cost of administering four monthly SMC cycles was $3·63 per child, ranging from $2·71 per child in Niger to $8·20 per child in The Gambia (table 3). The high cost of SMC in The Gambia was due to the relatively small population of children covered by the intervention and the relatively high total recurrent costs. The Gambia was the only country that recorded SMC coverage using Android mobile phones, which required training and remunerating of data recorders, many of whom were recruited from outside of the intervention areas. Compared with other countries, The Gambia had

	Burkina Faso	Chad	Guinea	Mali	Niger	Nigeria	The Gambia	Total
Non-governmental financial costs	4 216 563	1 755 718	1 386 686	3 123 431	2 143 028	4 476 871	581 387	17 683 684
SMC drugs and supplies	1 789 281	726 130	526 260	1 432 512	1 199 903	1 888 603	117 070	7 679 759
Meetings	161 301	179 520	36 754	123 227	8241	127 822	3840	640 706
Distributor per diem and travel	1 133 563	407 563	214 124	449 915	386 701	800 446	108 053	3 500 365
Direct supervisor per diem and travel	277 786	153 330	13 728	150 305	75 973	385 917	11 691	1 068 729
Other supervisor per diem and travel	154 025	72 060	108 838	236 898	92 957	171 296	68 457	904 529
Training	273 756	34 320	149 930	143 404	92 674	428 728	49 881	1 172 692
NGO programme management	215 088	39 364	138 311	305 918	130 650	388 547	116 280	1 334 158
Social mobilisation and behaviour change communication	144 607	113 367	112 038	230 844	68 405	148 060	97 437	914 759
Other costs	67 157	30 063	86 702	50 408	87 525	137 452	8680	467 987
Governmental financial costs	666 767	201 565	90 906	564 542	242 633	1 121 188	12 865	2 900 464
Distributor salaries	107 622	0	0	405 229	0	235 878	0	748 729
Supervisor salaries	138 136	96 336	39 325	120 270	87 114	490 967	4745	976 893
Programme management salaries	421,009	105 229	51 581	39 042	155 519	394 343	8120	1 174 843
Total financial costs	4 883 330	1 957 282	1 477 592	3 687 973	2 385 661	5 598 059	594 252	20 584 149
Volunteer opportunity costs	581 274	465 637	80 030	139 390	192 791	723 402	15 637	2 198 161
Volunteer distributors	581 274	414 185	80 030	139 390	179 843	637 248	15 637	2 047 607
Volunteer supervisors	0	51 452	0	0	12 948	86 154	0	150 555
Total costs	5 464 604	2 422 920	1 557 622	3 827 362	2 578 453	6 321 460	609 889	22 782 310

All costs are in 2016 US$. Costs in other currencies were converted, with $1 equal to 591 XOF, 591 XAF, 8347 GNF, 260 NGN, or 43 GMD. SMC=seasonal malaria chemoprevention. NGO=non-governmental organisation.

Table 2: **Recurrent economic costs of SMC intervention by resource type and funding source**

	Burkina Faso	Chad	Guinea	Mali	Niger	Nigeria	The Gambia
Non-governmental financial costs	2·92	2·80	3·17	2·68	2·25	2·84	7·82
SMC drugs and supplies	1·24	1·16	1·20	1·23	1·26	1·20	1·57
Meetings	0·11	0·29	0·08	0·11	0·01	0·08	0·05
Distributor per diem and travel	0·78	0·65	0·49	0·39	0·41	0·51	1·45
Direct supervisor per diem and travel	0·19	0·24	0·03	0·13	0·08	0·24	0·16
Other supervisor per diem and travel	0·11	0·11	0·25	0·20	0·10	0·11	0·92
Training	0·19	0·05	0·34	0·12	0·10	0·27	0·67
NGO programme management	0·15	0·06	0·32	0·26	0·14	0·25	1·56
Social mobilisation and behaviour change communication	0·10	0·18	0·26	0·20	0·07	0·09	1·31
Other costs	0·05	0·05	0·20	0·04	0·09	0·09	0·12
Governmental financial costs	0·46	0·32	0·21	0·48	0·25	0·71	0·17
Distributor salaries	0·07	0·00	0·00	0·35	0·00	0·15	0·00
Supervisor salaries	0·10	0·15	0·09	0·10	0·09	0·31	0·06
Programme management salaries	0·29	0·17	0·12	0·03	0·16	0·25	0·11
Total financial costs	3·38	3·12	3·38	3·16	2·50	3·55	7·99
Volunteer opportunity costs	0·40	0·74	0·18	0·12	0·20	0·46	0·21
Volunteer distributors	0·40	0·66	0·18	0·12	0·19	0·40	0·21
Volunteer supervisors	0·00	0·08	0·00	0·00	0·01	0·05	0·00
Total costs	3·78	3·86	3·56	3·28	2·71	4·01	8·20
Cost per child by distribution approach							
Door to door	3·64	3·86	3·56	..	4·05	..	8·20
Fixed point	12·22	..	..	4·73	..	..	..
Mobile point	..	..	..	2·89	..	..	..
Mixed methods	..	..	..	..	2·63	4·01	..

All costs are in 2016 US$. SMC=seasonal malaria chemoprevention. NGO=non-governmental organisation.

Table 3: **Recurrent economic costs per child for treatment with four doses of SMC**

higher associated SMC medicine costs for customs, clearance, warehousing, and distribution. The total cost of providing four monthly SMC cycles via door-to-door distribution ranged from $3·56 per child in Guinea to $4·05 per child in Niger, with The Gambia being an outlier at $8·20 per child. In the two countries where separate cost data were available for fixed-point distribution, the cost of administering four monthly SMC cycles was $4·73 per child in Mali, where this represented the major delivery strategy, and $12·22 per child in Burkina Faso, where this comprised less than 2% of treatments.

Among children younger than 5 years, SMC was estimated to have had a substantial effect on malaria morbidity and mortality in ACCESS-SMC areas. Based on the assumed 80% SMC monthly protective effectiveness rate, the intervention averted between 4·9 million and 7·1 million malaria cases, between 130 297 and 158 683 severe malaria cases, between 29 214 and 35 579 deaths, and between 835 512 and 1·02 million DALYs (3% discounted) in 2016 (table 4). Estimates for 85% SMC monthly effectiveness showed greater effects (table 4).

The cost per malaria case averted ranged from $2·91 in Niger to $30·73 in The Gambia (table 4). The cost per severe malaria case averted ranged from $119·63 in Niger to $506·00 in The Gambia. The cost per death averted ranged from $533·56 in Niger to $2256·92 in The Gambia. The cost per DALY averted (discounted) ranged from $18·66 in Niger to $78·91 in The Gambia. ICERs with undiscounted DALYs are also presented in table 4. In all countries, the cost per DALY averted (both discounted and undiscounted) was highly cost-effective.

The estimated recurrent economic costs saved were $66·0 million for all seven countries and ranged from $291 966 in The Gambia to $20·1 million in Nigeria (table 5). After deducting the costs of administering SMC, the net economic cost savings were $43·2 million, which greatly exceeded the economic costs of administering SMC in every country, with the exception of The Gambia. In Mali, for example, the economic cost of diagnosis and treatment saved of $14·5 million was more than four-times the economic costs of administering SMC of $3·8 million.

The sensitivity analyses are presented in the appendix (pp 33–37). Tornado diagrams for each country show the variation in ICERs (cost per DALY averted) around the base-case analysis. The low and high values used for sensitivity analyses reflect possible values for each parameter. Although all parameters affected the ICER, under all scenarios the ICER remained highly cost-effective in the seven countries. The cost per DALY

	Burkina Faso	Chad	Guinea	Mali	Niger	Nigeria	The Gambia	Total*
SMC effectiveness (80% effectiveness, lower incidence estimates)								
Malaria cases averted	913 043	236 182	283 659	1 086 056	886 767	1 514 044	19 846	4 939 596
Severe malaria cases averted	27 092	9640	6682	27 832	21 554	36 291	1205	130 297
Deaths averted	6074	2161	1498	6240	4833	8137	270	29 214
DALYs averted (3% discounting)	173 727	61 815	42 846	178 473	138 210	232 712	7729	835 512
DALYs averted (no discounting)	397 263	141 353	97 977	408 116	316 047	532 146	17 673	1 910 576
SMC effectiveness (85% effectiveness, lower incidence estimates)								
Malaria cases averted	970 109	250 943	301 387	1 153 935	942 189	1 608 672	21 086	5 248 321
Severe malaria cases averted	28 786	10 243	7100	29 572	22 901	38 559	1281	138 441
Deaths averted	6454	2296	1592	6630	5135	8645	287	31 040
DALYs averted (3% discounting)	184 585	65 678	45 524	189 627	146 848	247 257	8212	887 731
DALYs averted (no discounting)	422 092	150 188	104 101	433 624	335 800	565 405	18 778	2 029 987
ICERs for children <5 years (80% effectiveness, lower incidence estimates)								
Cost per malaria case averted	5·99	10·26	5·49	3·52	2·91	4·18	30·73	..
Cost per severe malaria case averted	201·70	251·34	233·11	137·51	119·63	174·19	506·00	..
Cost per death averted	899·62	1121·01	1039·72	613·33	533·56	776·90	2256·92	..
Cost per DALY averted (3% discounting)	31·46†	39·20†	36·35†	21·45†	18·66†	27·16†	78·91†	..
Cost per DALY averted (no discounting)	13·76†	17·14†	15·90†	9·38†	8·16†	11·88†	34·51†	..
2016 GDP per capita	627	664	662	780	364	2176	473	..

ICER=incremental cost-effectiveness ratio. SMC=seasonal malaria chemoprevention. DALY=disability-adjusted life-year. GDP=gross domestic product. *Data for individual countries might not add to totals due to rounding. †These values were considered highly cost-effective (defined as the cost per DALY averted being less than the 2016 GDP per capita).

Table 4: **Effectiveness and ICERs of SMC for children younger than 5 years**

	Burkina Faso	Chad	Guinea	Mali	Niger	Nigeria	The Gambia	Total
Total economic costs of administering SMC	5 464 604	2 422 920	1 557 622	3 827 362	2 578 453	6 321 460	609 889	22 782 310
Diagnosis and treatment economic costs saved	12 310 252	3 288 511	3 755 813	14 469 046	11 767 661	20 071 640	291 966	65 954 888
Net economic costs saved	6 845 648	865 591	2 198 191	10 641 683	9 189 209	13 750 180	−317 923	43 172 578

All costs are in 2016 US$. Cost savings are calculated assuming 80% effectiveness of SMC and lower incidence estimates. SMC=seasonal malaria chemoprevention.

Table 5: **Estimated cost savings for children younger than 5 years**

averted (both discounted and undiscounted) was highly cost-effective. Changes in MOH management costs had little effect on the ICER due to the small financial contribution of governments towards the intervention relative to donor contributions. Although changes to SMC protective effectiveness had little effect on the ICER, this one-way sensitivity analysis does highlight the potential for SMC to become less effective in the future for a number of reasons, including the development of resistance.

The sensitivity analysis also considered the effect of changes in care-seeking for children younger than 5 years with malaria. In the main analysis, we assumed that 60% of these children would be diagnosed and treated at a health facility (based on Tiono and colleagues[15]). However, in the sensitivity analysis (appendix p 37), a low value of 30% and a high value of 70% were considered. Under the low scenario, the net economic cost savings were $10·2 million, which exceeded the economic costs of administering SMC with the exception of Chad and The Gambia. In the high scenario, net savings were $54·2 million, which exceeded the cost of SMC administration, with the exception of The Gambia.

Discussion

This large-scale, multi-country study found SMC to be a low-cost and highly cost-effective intervention that contributes to substantial cost savings by reducing malaria diagnostic and treatment costs among children. The economic costs of one monthly dose ($0·68 to $2·05) and four cycles of SMC ($2·71 to $8·20 per child) are within the range of previous analyses. A 2016 study in Ghana by Nonvignon and colleagues[6] reported a cost (in 2015) of $22·53 per fully dosed child aged three to 59 months ($5·63 per monthly dose) in one region. A 2017 study by Pitt and colleagues[7] estimated a unit cost (in 2010) of between $0·38 and $2·74 per child aged up to 10 years with one monthly dose of SMC. The cost per malaria case averted ranged from $2·91 to $30·73, which is lower than the $107 reported by Nonvignon

and colleagues.[6] The cost per malaria death averted in our study ($533·56 to $2256·92) was lower in all seven countries compared with the equivalent figure of $3298, reported by Nonvignon and colleagues for Ghana, which was based on 80% monthly protective effectiveness. However, the two previous studies had differing methods of calculating costs and predicting effectiveness outcomes. Nonvignon and colleagues included capital items (eg, vehicles) in cost calculations,[6] and Pitt and colleagues considered only costs at the district level and below.[7]

To our knowledge, no previous study in sub-Saharan Africa has reported a cost per DALY averted for SMC. However, the results are also within the range of other malaria interventions. The median ICER per DALY averted was $27 (range $8·15 to $110) for insecticide-treated bednets, $143 ($135 to $150) for indoor residual spraying, and $24 ($1·08 to $44·24) for intermittent preventive treatment.[14] Based on our study, SMC is overall highly cost-effective in averting DALYs among children in areas of highly seasonal malaria transmission. However, with the increasing reduction of malaria-related mortality globally, economic analyses should focus more on malaria cases and DALYs than on deaths to inform decision making.[6,16]

Interventions such as SMC, insecticide-treated bednets, and intermittent preventive treatment should also be appraised for their level of affordability, especially given the push for more stringent cost-effectiveness thresholds.[17] The SMC intervention analysed in this study was funded by Unitaid in these seven countries, with relatively small financial contributions from governments. In the absence of future donor funding for SMC, governments might be unable to sustain the attained levels of SMC coverage and reduction in malaria burden.

The overall cost-effectiveness of SMC would probably be improved by greater intervention coverage (ie, treating more children and ensuring a higher proportion receive the full course), as evidenced by the coverage survey data. In The Gambia, the relatively high fixed costs of implementation and the small population of children covered with SMC contributed to a high ICER. SMC medicine shortages contributed to low coverage in the first cycle in Nigeria and the fourth cycle in Chad. Nevertheless, in the absence of major funding from Unitaid, the levels of SMC coverage and corresponding cost-effectiveness of the intervention might have been different.

Although the study presents the costs of different SMC approaches (eg, door-to-door or fixed-point distribution), these were considered complimentary in countries which utilised multiple distribution methods, with each having their own benefits. Door-to-door distribution probably provides better access to the medication for people from lower socioeconomic quintiles and those living in hard-to-reach areas than other distribution methods. Although reaching rural areas might be more expensive and less cost-effective, these populations might receive the most benefit from the intervention, given issues of access to quality malaria diagnosis and treatment services. Fixed-point distribution at a health facility provides an opportunity for children to be screened by a health provider and receive other preventive services (eg, immunisations). Because health facility personnel are remunerated regardless of whether they provide SMC, the intervention might not necessarily be considered an additional cost but rather an opportunity cost, because it reduces the time that they have available to provide other services. Nevertheless, reductions in malaria incidence due to SMC probably would reduce the time required for diagnosing and treating cases, thereby freeing up their time for other activities.

This study further shows that SMC can produce substantial savings in terms of averted diagnosis and treatment costs when compared with routine care. These estimates assume the same unit financial and economic costs for treating uncomplicated and severe malaria in all seven countries. Depending on the proportion of malaria cases treated at a health facility, these estimates could represent an overestimation or underestimation of the actual cost savings. Nevertheless, the cost of SMC implementation in most countries does not represent an added cost, but rather an investment that could result in savings to the health system. The total cost saving for diagnosis and treatment in 2016 was estimated to be $66·0 million in the seven countries and the net economic cost savings were $43·2 million after deducting the costs of administration ($22·8 million). These savings could free up much-needed resources to expand SMC to the estimated 13·6 million children living in eligible geographical areas, of which more than 9 million live in Nigeria.[18]

However, the study did have a number of limitations. We excluded the costs of several key programmatic components, such as some capital costs (eg, NGO and MOH office buildings and vehicles) and start-up costs, the majority of which were incurred in previous years. Start-up costs (accounting for 4·39% of total costs) comprised time and resources for the preparation of reporting tools and training materials, stakeholder meetings, and the development of behaviour-change communication messaging (eg, radio and print advertising). The cost of pharmacovigilance systems for drug safety monitoring, coverage surveys, and monitoring of drug resistance was also excluded.

Moreover, the study was done from the programmatic perspective and did not measure the economic costs experienced by children and families accessing SMC (eg, the value of time taken to access care and out-of-pocket costs) nor the associated costs for treating children with secondary effects, although cases were reportedly low.[11] We expect that families would experience considerable

savings related to costs averted for accessing and paying out of pocket for malaria diagnosis and treatment, especially in countries which have user fees in place. Although the study obtained time allocation estimates (eg, from SMC distributors) through interviews, direct observation would have been preferable, but it was not possible due to the timing of data collection.

In addition, as indicated in the methods, the study presents the cost per child based on the equivalent number of children who received four doses in each country. However, this does not represent the true cost of a fully adherent child, as evidenced by the coverage survey data on the percentage of children who received the recommended four monthly doses of SMC in each country.

Although there is uncertainty around the modelled predictions of malaria incidence, conservative estimates were used to avoid overestimating the impact of SMC. Health management information system data indicate substantial reductions in malaria cases at health facilities since the introduction of SMC;[9] however, these data do not provide reliable estimates of numbers of cases averted, due to the large proportion of people with malaria that do not present to health facilities.

The cost-effectiveness of integrating SMC with other services could not be determined due to the absence of reliable data. In Burkina Faso, Mali, and Niger, SMC was reportedly integrated with the provision of rapid diagnostic tests for malaria, malaria treatment, malnutrition screening, and referrals. Because SMC is one of the few platforms that reaches vulnerable children younger than 5 years simultaneously on a large scale, further research could help to identify opportunities for integration[19] and improve its cost-effectiveness.[5]

In conclusion, this study is the first to estimate the cost-effectiveness and cost savings of a large scale, multi-country SMC campaign targeting children younger than 5 years in the Sahel region of sub-Saharan Africa. Our results show that SMC is both cost-effective and cost saving in the seven countries evaluated.

Contributors

CG, JN, MC, PM, and DC designed the study. CG, JN, and FB collected cost data. CG, JN, and DC analysed and interpreted cost, cost-effectiveness, and cost-saving data. MC, PM, and PW modelled the effectiveness data and wrote the section on predicting malaria cases and deaths averted by SMC. JN modelled the DALYs averted and wrote up the results. CG wrote the first draft of the manuscript. All authors interpreted the data and contributed to the manuscript.

Declaration of interests

JN and FB report personal fees from Management Sciences for Health, during the conduct of the study. PW reports personal fees from The Global Fund, outside of the submitted work. All other authors declare no competing interests.

Data sharing

All data relevant to the study are included in the Article or uploaded as supplementary information.

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