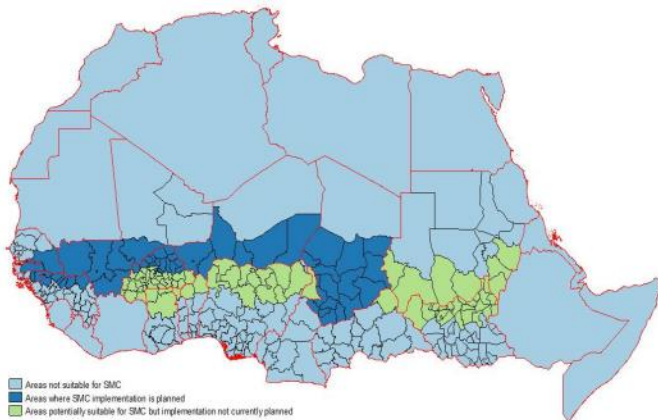


Seasonal Malaria Chemo-prevention (SMC)

From Doctoral Research to Health Policy and Regional Scaling-Up

Dr. Badara Cissé
Med. epidemiologist



Objectives



- Define the concept and recall natural history
- Summarise some key findings that led to the WHO recommendation
- Pilot large-scale implementation in Niakhar, Senegal
- SMC in 2016

From IPT to SMC



Intermittent preventive treatment of malaria was initially recommended for the prevention of malaria during pregnancy (IPT) using SP



Intermittent Preventive Treatment of malaria in infants (IPTi) with antimalarial medicines delivered through the Expanded Programme on Immunisation (EPI)

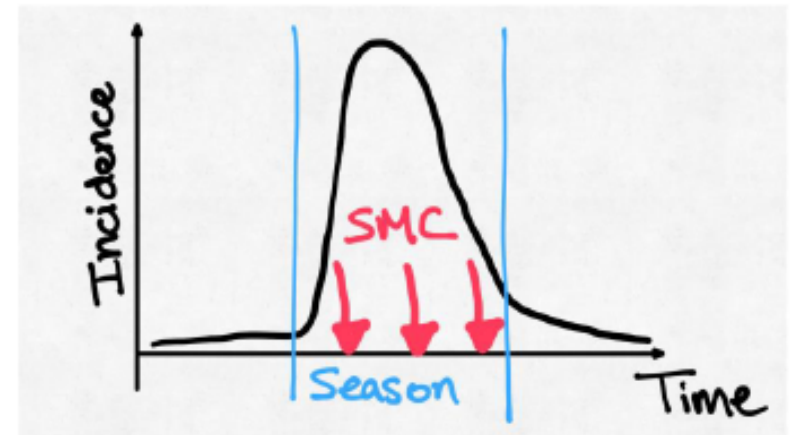


Intermittent preventive treatment of malaria was extended to older children (IPTc)

Renamed Seasonal Malaria Chemoprevention (SMC) by the WHO in 2011

Definition

- SMC is the intermittent administration of full treatment courses of an antimalarial medicine during the malaria season to prevent malaria illness and deaths
 - The objective is to maintain therapeutic drug concentrations in the blood throughout the period of greatest malaria risk
- *Children aged 3 - 59 months,*
- *Amodiaquine plus sulfadoxine-pyrimethamine (AQ+SP)*
- *Monthly administration*
- *Given from the start of the transmission season*
- *Maximum of four doses per season*



Efficacy in Randomised controlled trial

Articles

Niakhar I

1.00

0.75

0.50

0.25

0.00

Seasonal intermittent preventive treatment with artesunate and sulfadoxine-pyrimethamine for prevention of malaria in Senegalese children: a randomised, placebo-controlled, double-blind trial

Badara Cissé, Cheikh Sokhna, Denis Boulanger, Jacqueline Milet, El Hadj Bâ, Keshana Richardson, Rachel Hallett, Colin Sutherland, Kirsten Simondon, François Simondon, Neal Alexander, Oumar Gaye, Geoffrey Targett, Jo Lines, Brian Greenwood, Jean-François Trape

Summary

Background In the Sahel and sub-Saharan regions of Africa, malaria transmission is highly seasonal. During a short period of high malaria transmission, mortality and morbidity are high in children under age 5 years. We assessed the efficacy of seasonal intermittent preventive treatment—a full dose of antimalarial treatment given at defined times without previous testing for malaria infection.

Methods We did a randomised, placebo-controlled, double-blind trial of the effect of intermittent preventive treatment on morbidity from malaria in three health-care centres in Niakhar, a rural area of Senegal. 1136 children aged 2–59 months received either one dose of artesunate plus one dose of sulfadoxine-pyrimethamine or two placebos on three occasions during the malaria transmission season. The primary outcome was a first or single episode of clinical malaria detected through active or passive case detection. Primary analysis was by intention-to-treat. This study is registered with ClinicalTrials.gov, number NCT00132561.

Findings During 13 weeks of follow-up, the intervention led to an 86% (95% CI 80–90) reduction in the occurrence of clinical episodes of malaria. With passive case detection, protective efficacy against malaria was 86% (77–92), and when detected actively was 86% (78–91). The incidence of malaria in children on active drugs was 308 episodes per 1000 person-years at risk, whereas in those on placebo it was 2250 episodes per 1000 person-years at risk. 13 children were not included in the intention-to-treat analysis, which was restricted to children who received a first dose of antimalarial or placebo. There was an increase in vomiting in children who received the active drugs, but generally the intervention was well tolerated.

Interpretation Intermittent preventive treatment could be highly effective for prevention of malaria in children under 5 years of age living in areas of seasonal malaria infection.

Introduction

According to the World Health Organization, 90% of deaths from malaria are in Africa and mostly in children under 5 years of age.¹ Efforts to control this disease in Africa have been hindered by the spread of resistance to chloroquine and, more recently, to sulfadoxine-pyrimethamine.^{2,3} In Senegal, the yearly mortality rate from malaria in children has increased substantially since the beginning of the 1990s.⁴ This rise, associated with the emergence of chloroquine resistance, has been recorded in three regions of the country with different rates of malaria endemicity.⁵ The loss of effective and affordable drugs for the treatment of malaria has focused attention not only on the need for new antimalarial drugs,⁶ but also on the need for new ways to prevent infection, especially in children under 5 years.

Several studies have shown that African children can be protected effectively from the consequences of malaria by chemoprophylaxis, with use of anti-malarial drugs on a

reduced overall mortality in children by about 35%.¹¹ However, this approach to malaria control is difficult to sustain and there have been concerns that it would contribute to the spread of drug resistance.¹²

Intermittent preventive treatment differs from chemoprophylaxis because members of an at risk population are given a full therapeutic dose of treatment at set times, whether or not they are known to be infected. By contrast with chemoprophylaxis, drug concentrations might fall below parasite inhibitory concentrations between drug administrations. Such preventive treatment was first shown to be an effective approach for the control of malaria in pregnant women. In Malawi, this treatment method with sulfadoxine pyrimethamine reduced placental malaria by 72%.¹³ Subsequent studies have shown the beneficial effect of such treatment on severe anaemia in pregnant women and on the incidence of low birthweight.^{14,15}

A similar approach has been adapted to the prevention

Lancet 2006; 367: 659–67

Institut de Recherche pour le Développement, Dakar, Senegal (C Sokhna PhD, D Boulanger PhD, J Milet PhD, E H Bâ MSc, K Simondon MD, F Simondon MD, J-F Trape MD); Université Cheikh Anta Diop de Dakar, Senegal (Prof O Gaye MD); London School of Hygiene & Tropical Medicine, London, UK (B Cissé MD, K Richardson PhD, N Alexander PhD, C Sutherland PhD, R Hallett PhD, Prof G Targett DSc, J Lines PhD, Prof B M Greenwood MD)

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A Trial of the Efficacy, Safety and Impact on Drug Resistance of Four Drug Regimens for Seasonal Intermittent Preventive Treatment for Malaria in Senegalese Children

Cheikh Sokhna^{1*}, Badara Cissé², El Hadj Bâ¹, Paul Milligan^{3*}, Rachel Hallett³, Colin Sutherland³, Oumar Gaye², Denis Boulanger¹, Kirsten Simondon¹, François Simondon¹, Geoffrey Targett³, Jo Lines³, Brian Greenwood³, Jean-François Trape¹

¹ Institut de Recherche pour le Développement, Dakar, Senegal, ² Université Cheikh Anta Diop de Dakar, Dakar, Senegal, ³ London School of Hygiene & Tropical Medicine, London, United Kingdom

Summary: In the Sahel, most malaria deaths occur among children 1–4 years old during a short transmission season. A trial of seasonal intermittent preventive treatment (IPT) with sulfadoxine-pyrimethamine (SP) and a single dose of artesunate (AS) showed an 86% reduction in the incidence of malaria in Senegal but this may not be the optimum regimen. We compared this regimen with three alternatives. **Methods.** 2102 children aged 6–59 months received either one dose of SP plus one dose of AS (SP+1AS) (the previous regimen), one dose of SP plus 3 daily doses of AS (SP+3AS), one dose of SP plus three daily doses of amodiaquine (AQ) (SP+3AQ) or 3 daily doses of AQ and AS (3AQ+3AS). Treatments were given once a month on three occasions during the malaria transmission season. The primary end point was incidence of clinical malaria. Secondary end-points were incidence of adverse events, mean haemoglobin concentration and prevalence of parasites carrying markers of resistance to SP. **Findings.** The incidence of malaria, and the prevalence of parasitaemia at the end of the transmission season, were lowest in the group that received SP+3AQ: 10% of children in the group that received SP+1AS had malaria, compared to 9% in the SP+3AS group (hazard ratio HR 0.90, 95%CI 0.60, 1.36); 11% in the 3AQ+3AS group, HR 1.1 (0.76–1.7); and 5% in the SP+3AQ group, HR 0.50 (0.30–0.81). Mutations associated with resistance to SP were present in almost all parasites detected at the end of the transmission season, but the prevalence of *Plasmodium falciparum* was very low in the SP+3AQ group. **Conclusions.** Monthly treatment with SP+3AQ is a highly effective regimen for seasonal IPT. Choice of this regimen would minimise the spread of drug resistance and allow artemisinins to be reserved for the treatment of acute clinical malaria. **Trial Registration.** Clinicaltrials.gov NCT00132548

Citation: Sokhna C, Cissé B, Bâ EH, Milligan P, Hallett R, et al (2008) A Trial of the Efficacy, Safety and Impact on Drug Resistance of Four Drug Regimens for Seasonal Intermittent Preventive Treatment for Malaria in Senegalese Children. PLoS ONE 3(1): e1471. doi:10.1371/journal.pone.0001471

INTRODUCTION

In Sub-Saharan Africa, malaria remains the most common cause of morbidity and mortality and is still estimated to cause one million deaths a year, primarily in young children [1]. Insecticide-treated bednets (ITNs) can reduce mortality and morbidity from malaria substantially [2] but they are only partially effective and achieving high levels of coverage with ITNs has proved difficult. Other preventive strategies are needed.

Administration of antimalarial chemoprophylaxis to the whole paediatric population can reduce malaria morbidity and all-causes mortality substantially [3] but this approach to malaria control has not been adopted widely because of concerns over the enhancement of drug resistance, impairment of naturally acquired immunity and difficulties in implementation. Intermittent preventive treatment (IPT), the administration of an antimalarial drug or drug combination in curative doses at specific time points (for example antenatal clinic visits or visits for routine immunisation) offers a potential way of achieving some of the gains provided by chemoprophylaxis whilst limiting some of its potential drawbacks [4]. Drugs used for IPT must be very safe as well as effective. Several studies have shown that IPT given with routine immunisation during the first year of life is effective in reducing the incidence of clinical malaria and of anaemia [5–9]. In Tanzania, approximately 50% protection against clinical attacks of malaria and anaemia was achieved during the first year of life using sulfadoxine-pyrimethamine (SP) and this protection was sustained during the following year in the absence of any further drug administration [5,6]. A second study undertaken in Tanzania

in which amodiaquine (AQ) was given routinely at growth monitoring visits achieved similar results [7].

However, more recent studies of IPT with SP conducted in Ghana and Mozambique have given less marked reductions in the incidence of malaria or anaemia and no persistence of protection beyond the period of drug administration [8,9]. Further trials of IPT in infants using alternative drugs to SP are under way in Kenya and Tanzania under the auspices of the IPTi consortium [10]. Sufficient data should have been collected within the next year to determine whether IPT in infants is sufficiently effective to warrant introduction into the routine expanded programme of immunisation (EPI).

Academic Editor: Stephen Rogerson, Royal Melbourne Hospital, Australia

Received: July 12, 2007; **Accepted:** October 1, 2007; **Published:** January 23, 2008

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Funding: The trial was funded by the Bill and Melinda Gates Foundation. The sponsor played no role in the design and conduct of the study or preparation of the paper.

Competing Interests: The authors have declared that no competing interests exist.

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SP+AQ
superior

SP+AQ
superior

DHA+PQ
superior

Malaria Intermittent

5

Comparator
better

7

Randomized Trial of Pi
Preventive Treatment i

-7

-5

New regimen
better

Amodiaquine dosage



Risk of mild adverse
dose per kg bodyw

ith

ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, Mar. 2010, p. 1265–1274
0066-4804/10/\$12.00 doi:10.1128/AAC.01161-09
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Vol. 54, No. 3

Amodiaquine Dosage and Tolerability for Intermittent Preventive Treatment To Prevent Malaria in Children^{††}

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Received 16 August 2009/Returned for modification 2 December 2009/Accepted 2 January 2010

Sulfadoxine-pyrimethamine with amodiaquine (SP-AQ) is a highly efficacious regimen for intermittent preventive treatment to prevent malaria in children (IPTc), but the amodiaquine component is not always well tolerated. We determined the association between amodiaquine dosage by body weight and mild adverse events (AEs) and investigated whether alternative age-based regimens could improve dosing accuracy and tolerability, using data from two trials of IPTc in Senegal, one in which AQ dose was determined by age and the other in which it was determined by weight category. Both dosage strategies resulted in some children receiving AQ doses above the recommended therapeutic range. The odds of vomiting increased with increasing amodiaquine dosage. In one study, incidence of fever also increased with increasing dosage. Anthropometric data from 1,956 children were used to predict the dosing accuracy of existing and optimal alternative regimens. Logistic regression models describing the probability of AEs by dosage were used to predict the potential reductions in mild AEs for each regimen. Simple amendments to current AQ dosing schedules based on the child's age could substantially increase dosing accuracy and thus improve the tolerability of IPTc using SP-amodiaquine in situations where weighing the child is impractical.

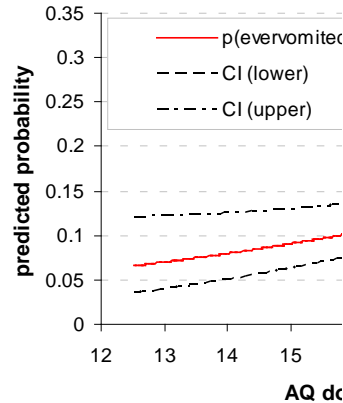
Relatively minor adverse reactions to antimalarials that may be acceptable when malaria illness is being treated may not be acceptable when drugs are used on a large scale for intermittent preventive treatment in children (IPTc), when the majority of recipients will be healthy. The response of children and their parents to adverse reactions, even those relatively minor in nature, could limit the uptake of IPTc as a strategy. It is, therefore, important to minimize the side effects associated with this intervention.

Sulfadoxine-pyrimethamine combined with amodiaquine (SP-AQ) has been identified as a highly efficacious regimen for treatment of malaria (4, 8, 11, 23–26) and for IPT (5, 14). However, when used for IPT in children, SP-AQ has been associated with an increased incidence of mild adverse events, particularly vomiting and fever, in the days following the IPT course (5, 14). One answer to this problem would be to use other antimalarials as the partner drug to SP, which has been shown extensively to be safe and well tolerated when used for intermittent preventive treatment (1, 6). Long-acting antimalarials are preferable to artemisinins for IPT because they provide a longer period of posttreatment prophylaxis, which is central to the protection given by IPT (4a, 19). Piperaquine has been identified as a promising partner drug (5) (K. Bojang et al., unpublished data). However, SP-piperaquine is currently not licensed as a combination for use in IPT and there may be

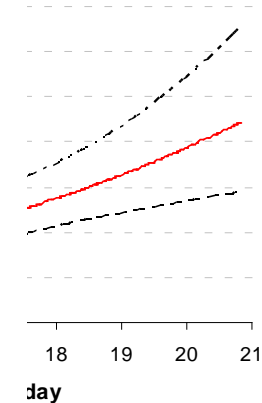
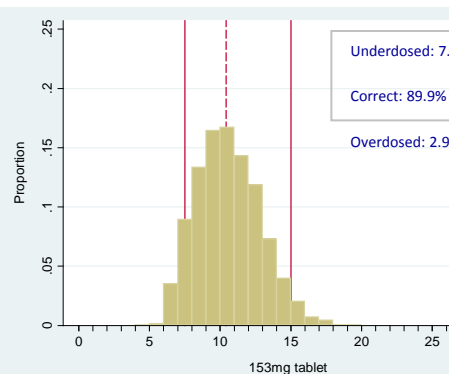
some delay in obtaining sufficient safety and pharmacokinetic data to allow deployment of this combination. Any measures that can improve the tolerability of SP-AQ for use in the meantime could therefore be beneficial.

One way in which the tolerability of SP-AQ might be improved is by ensuring that children receive as accurate a dose as possible. The recommended dose for a course of amodiaquine is 30 mg amodiaquine base/kg body weight over 3 days, i.e., 10 mg/kg/day (22). Dosing by weight is therefore the ideal approach, but limitations in resources and training may make this impractical in resource-poor areas (2, 9). Weighing children may be particularly problematic with a large-scale preventive intervention such as IPTc, in which many children will be treated in a short space of time and mobility of health workers may be important for successful delivery (Bojang et al., unpublished data). Development of an accurate dose-for-age schedule would thus be advantageous. Dose-for-age has already been developed for amodiaquine as part of a fixed dose combination with artesunate used for treatment of malaria cases (13, 16), but the priorities may be different for IPT because most children will not be unwell when they are treated. Regimens could be developed specifically for use in IPT.

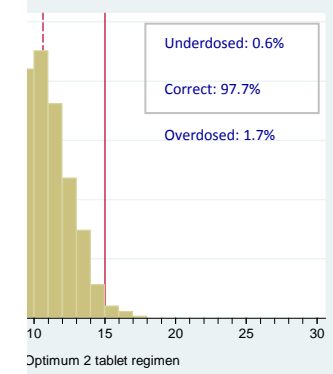
The regimen used in previous and ongoing trials of IPTc in Senegal consists of one 200-mg AQ tablet for children aged 2 years or over and half a 200-mg tablet for younger children (5; www.clinicaltrials.gov, identifier NCT00712374). Since health workers are used to dichotomizing the dose given to children at 2 years of age, replacing the 200-mg tablet with one with lower AQ content might be a simple way to improve dosing accuracy. One option would be to use a 153-mg AQ tablet that is currently available for treatment. An alternative age-based regimen for amodiaquine was developed using a large anthropo-



Select age-based
who receive dose



er of children
15 mg/kg/day



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[†] Published ahead of print on 11 January 2010.

^{††} The authors have paid a fee to allow immediate free access to this article.

SMC provides substantial protection against malaria in children already using LLINs in Mali and Burkina faso

	LLIN + Placebo		LLIN + SMC			
	No. of cases	Incidence rate (95% CI)	No. of cases	Incidence rate (95% CI)	PE (95%CI)	P value
Malaria (parasitaemia > 5000)	1656	2.38 (2.27-2.50)	458	0.61 (0.56-0.67)	75 (72-77)	<0.001
Severe malaria	22	0.002 (0.001 – 0.003)	4	0.0004 (0.0001 – 0.0011)	82 (48–94)	0.002
All-cause hospital admissions	45	0.056 (0.042– 0.075)	27	0.033 (0.023 – 0.049)	41 (5–63)	0.03

Konate and al, et al. (2011) Intermittent Preventive Treatment of Malaria Provides Substantial Protection against Malaria in Children Already Protected by an Insecticide-Treated Bednet in Burkina Faso: A Randomised, Double-Blind, Placebo-Controlled Trial. **PLoS Med 8(2): e1000408. doi:10.1371 / journal. pmed.1000408**

Meta analysis & impact on clinical malaria

OPEN ACCESS Freely available online



A Systematic Review and Meta-Analysis of the Efficacy and Safety of Intermittent Preventive Treatment of Malaria in Children (IPTc)

Anne L. Wilson*, on behalf of the IPTc Taskforce[†]

London School of Hygiene and Tropical Medicine, London, United Kingdom

Study

ID

Kweku, 2008, AS+AC

Cisse, 2006, SP+AS

Bojang, 2010, DHA+f

Bojang, 2010, SP+PC

Bojang, 2010, SP+AC

Dicko, 2011, SP+AQ

Konate, 2011, SP+AC

Sesay, 2011, SP+AQ

Zongo, unpub SPAQ

Zongo, unpub DHAP

D+L Overall (I-squar

I-V Overall

NOTE: Weights are fr

Abstract

Background: Intermittent preventive treatment of malaria in children less than five years of age (IPTc) has been investigated as a measure to control the burden of malaria in the Sahel and sub-Saharan areas of Africa where malaria transmission is markedly seasonal.

Methods and Findings: IPTc studies were identified using a systematic literature search. Meta-analysis was used to assess the protective efficacy of IPTc against clinical episodes of falciparum malaria. The impact of IPTc on all-cause mortality, hospital admissions, severe malaria and the prevalence of parasitaemia and anaemia was investigated. Three aspects of safety were also assessed: adverse reactions to study drugs, development of drug resistance and loss of immunity to malaria. Twelve IPTc studies were identified: seven controlled and five non-controlled trials. Controlled studies demonstrated protective efficacies against clinical malaria of between 31% and 93% and meta-analysis gave an overall protective efficacy of monthly administered IPTc of 82% (95%CI 75%–87%) during the malaria transmission season. Pooling results from twelve studies demonstrated a protective effect of IPTc against all-cause mortality of 57% (95%CI 24%–76%) during the malaria transmission season. No serious adverse events attributable to the drugs used for IPTc were observed in any of the studies. Data from three studies that followed children during the malaria transmission season in the year following IPTc administration showed evidence of a slight increase in the incidence of clinical malaria compared to children who had not received IPTc.

Conclusions: IPTc is a safe method of malaria control that has the potential to avert a significant proportion of clinical malaria episodes in areas with markedly seasonal malaria transmission and also appears to have a substantial protective effect against all-cause mortality. These findings indicate that IPTc is a potentially valuable tool that can contribute to the control of malaria in areas with markedly seasonal transmission.

Citation: Wilson AL, on behalf of the IPTc Taskforce (2011) A Systematic Review and Meta-Analysis of the Efficacy and Safety of Intermittent Preventive Treatment of Malaria in Children (IPTc). PLoS ONE 6(2): e16976. doi:10.1371/journal.pone.0016976

Editor: David Diemert, The George Washington University Medical Center, United States of America

Received: October 14, 2010; **Accepted:** January 12, 2011; **Published:** February 14, 2011

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Funding: This work was supported by a grant to the London School of Hygiene & Tropical Medicine from the Bill & Melinda Gates Foundation (Grant number: OPP51371). The funders had no role in study design, data collection and analysis, decision to publish or preparation of the manuscript.

Competing Interests: The authors have declared that no competing interests exist.

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[†] Membership of the IPTc Taskforce is provided in the Acknowledgments.

Introduction

Intermittent preventive treatment of malaria (IPT) refers to the administration of a full therapeutic course of an anti-malarial drug to the whole of a population at risk, whether or not they are known to be infected, at specific times, with the aim of preventing mortality or morbidity from malaria [1]. IPT with sulphadoxine-pyrimethamine (SP) is recommended by the WHO for use in pregnant women (IPTp) and has recently been recommended by the WHO for use in infants (IPTi), delivered alongside vaccines within the context of the routine Expanded Programme on Immunisation [2]. The decision by WHO to recommend IPTi in areas where there is a significant malaria burden in infants and

clinical malaria [3]. In areas of markedly seasonal malaria transmission, such as the Sahel and sub-Saharan regions of Africa, the main burden of malaria is in older children rather than infants, and the risk of clinical malaria is restricted largely to a few months each year [4,5]. In such areas, administration of IPT to children several times during the seasonal peak in malaria transmission (IPTc) has been investigated as a method of preventing malaria.

A Cochrane review published in 2008 reviewed the efficacy and safety of chemoprophylaxis and IPT in children [6]. However, although there is some overlap in the mechanism of protection provided by chemoprophylaxis and IPT, these two approaches set out to produce different blood concentration profiles and the efficacy and safety of the two methods may differ. Since the

Pilot large scale implementation in Senegal



Nb de postes de santé							Total		
	9	9	9	9	9	9	54		
Mar-May 2008	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	54		
Sep-Nov 2008	<input checked="" type="checkbox"/>						9	Administration children aged 3-60 months	
2009	<input checked="" type="checkbox"/> <input checked="" type="checkbox"/> <input checked="" type="checkbox"/>						27	Administration children aged 3-120 months	
2010	<input checked="" type="checkbox"/> <input checked="" type="checkbox"/> <input checked="" type="checkbox"/> <input checked="" type="checkbox"/> <input checked="" type="checkbox"/>						45		

☐ census ☒ IPTc



Pilot implementation in Senegal

790948 documented doses



	3-59mois 2008	3-120mois 2009	3-120 mois 2010
Postes de santé	9	27	45
Nb moyen de relais	195	585	830
Nb d'enfants vus			
Sep	13882	89347	154013
Oct	13914	89405	157602
Nov	15397	91694	159667
Moyenne Nb d'enfants/Relais	74	154	189

Intervention coverages



	2008 (N=1018)		2009 (N=3226)	
Number of doses	Coverage	95%CI	Coverage	95%CI
0	3.9%	(2.5%- 5.2%)	5.7%	(4.5%-6.9%)
1	0.75%	(0.15%- 1.4%)	1.6%	(1.0%-2.2%)
2	3.0%	(1.2%- 4.7%)	3.2%	(1.9%-4.4%)
3	92.4%	(90.2%- 94.6%)	89.6%	(87.6%-91.5%)

Summary of findings



- No evidence of serious adverse effects due to SMC drugs after administration of 791,000 doses
- Excellent coverage and adherence to door-to-door strategy
- Estimated financial cost at 0.5 \$
- Purchasing drugs and CHWs payments are the largest components of the cost
- Economy by integrating interventions

Scale-up Efficiency (69%)



Direct effects of

Indirect effects of



RESEARCH ARTICLE

Effectiveness of Seasonal Malaria Chemoprevention in Children under Ten Years of Age in Senegal: A Stepped-Wedge Cluster-Randomised Trial

Badara Cissé^{1,2}, El Hadj Ba^{2,3}, Cheikh Sokhna³, Jean Louis NDiaye¹, Jules F. Gomis¹, Yankhoba Dial⁴, Catherine Pitt², Mouhamed NDiaye¹, Matthew Cairns², Ernest Faye¹, Magatte NDiaye¹, Aminata Lo¹, Roger Tine¹, Sylvain Faye¹, Babacar Faye¹, Ousmane Sy¹, Lansana Konate¹, Ekoue Kouevijidin³, Clare Flach², Ousmane Faye¹, Jean-Francois Trape³, Colin Sutherland², Fatou Ba Fall⁴, Pape M. Thior⁴, Oumar K. Faye⁴, Brian Greenwood², Oumar Gaye¹, Paul Milligan^{2*}

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OPEN ACCESS

Citation: Cissé B, Ba EH, Sokhna C, NDiaye JL, Gomis JF, Dial Y, et al. (2016) Effectiveness of Seasonal Malaria Chemoprevention in Children under Ten Years of Age in Senegal: A Stepped-Wedge Cluster-Randomised Trial. *PLoS Med* 13(11): e1002175. doi:10.1371/journal.pmed.1002175

Academic Editor: Abdulsalam Mohamed Noor, Kenya Medical Research Institute - Wellcome Trust Research Programme, KENYA

Received: September 25, 2015

Accepted: October 6, 2016

Published: November 22, 2016

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Data Availability Statement: Demographic Surveillance System data, malaria incidence data, and individual-level survey data, are available at <http://dx.doi.org/10.17037/DATA.117>. Requests for access will be reviewed by a Data Access Committee to ensure use of the data protect participant privacy according to the terms of participant consent and ethics committee approval.

Funding: This study was funded by the Bill and Melinda Gates Foundation, grant number 40099.

Abstract

Background

Seasonal Malaria Chemoprevention (SMC) with sulfadoxine-pyrimethamine (SP) plus amodiaquine (AQ), given each month during the transmission season, is recommended for children living in areas of the Sahel where malaria transmission is highly seasonal. The recommendation for SMC is currently limited to children under five years of age, but, in many areas of seasonal transmission, the burden in older children may justify extending this age limit. This study was done to determine the effectiveness of SMC in Senegalese children up to ten years of age.

Methods and Findings

SMC was introduced into three districts over three years in central Senegal using a stepped-wedge cluster-randomised design. A census of the population was undertaken and a surveillance system was established to record all deaths and to record all cases of malaria seen at health facilities. A pharmacovigilance system was put in place to detect adverse drug reactions. Fifty-four health posts were randomised. Nine started implementation of SMC in 2008, 18 in 2009, and a further 18 in 2010, with 9 remaining as controls. In the first year of implementation, SMC was delivered to children aged 3–59 months; the age range was then extended for the latter two years of the study to include children up to 10 years of age. Cluster sample surveys at the end of each transmission season were done to measure coverage of SMC and the prevalence of parasitaemia and anaemia, to monitor molecular markers of drug resistance, and to measure insecticide-treated net (ITN) use.

95%CI)

.35)

.79)

Policy process



Meeting on IPTc – Dakar 2008

- *Safety,*
- *Can it be delivered*
- *Rebound*
- *Added benefit if children are using ITNs*

Informal consultation WHO - Geneva 2010

- *costs of delivery*
- *Implementation where there is good efficacy evidence*
- *Size of population that stands to benefit*
- *Distinction between prevention and treatment*
- *Treatment only and always after a RDT+*
- *Different drugs for prevention and treatment*

TEG 2011 WHO - Geneva 2012

MPAC WHO - Geneva 2012

Endorsement WHO - Geneva 2012

WHO SMC recommendation



World Health Organization
GLOBAL MALARIA PROGRAMME

WHO Global Malaria Programme

**WHO Policy Recommendation:
Seasonal Malaria Chemoprevention (SMC)
for *Plasmodium falciparum* malaria control in highly seasonal transmission areas
of the Sahel sub-region in Africa**

March 2012

Background

Malaria remains a leading cause of ill health, causing an estimated 216 million cases of clinical malaria and 655 thousand deaths in 2010^a. More than 85% of malaria cases and 90% of malaria deaths occur in Africa south of the Sahara, here the vast majority of cases and deaths occur in young children.

Across the Sahel sub-region most childhood malaria mortality and morbidity occurs during the rainy season, which is generally short. Giving effective malaria treatment at intervals during this period has been shown to prevent illness and death from malaria in children.

Key interventions currently recommended by WHO for the control of malaria are the use of insecticide treated nets (ITNs) and/or indoor residual spraying (IRS) for vector control, and prompt access to diagnostic testing of suspected malaria and treatment of confirmed cases. Additional interventions which are recommended in areas of high transmission for specific high risk groups include Intermittent Preventive Treatment in pregnancy (IPTp), and Intermittent Preventive Treatment in infancy (IPTi).

With the changing epidemiology of malaria, there is a progressive paradigm shift from a "one size fits all" approach, to the targeting of malaria control strategies to specific populations and/or locations for maximal effectiveness. In keeping with this approach, WHO is now recommending a new intervention against *Plasmodium falciparum* malaria: Seasonal Malaria Chemoprevention (SMC). This intervention has been shown to be effective, cost-effective, safe, and feasible for the prevention of malaria among children less than 5 years of age in areas with highly seasonal malaria transmission.

Seasonal malaria chemoprevention^b (SMC), previously referred to as Intermittent Preventive Treatment in children (IPTc), is defined as the intermittent administration of full treatment courses of an antimalarial medicine during the malaria season to prevent malarial illness with the objective of maintaining therapeutic antimalarial drug concentrations in the blood throughout the period of greatest malarial risk.

^a World Malaria Report 2011. Geneva, World Health Organization, 2011 (ISBN 978 92 4 156440 1)
http://www.who.int/malaria/world_malaria_report_2011/2789241564403_eng.pdf
^b The word chemoprevention is used in SMC because the intervention comprises the administration of full curative treatment courses as opposed to chemoprophylaxis, which usually involves administration of sub-therapeutic doses.

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SEASONAL MALARIA CHEMOPREVENTION WITH SULFADOXINE- PYRIMETHAMINE PLUS AMODIAQUINE IN CHILDREN

A FIELD GUIDE

Field implementation guide

Policy recommendation



- Target areas for implementation is the Sahel sub-region where:
 - malaria transmission is highly seasonal and the majority of clinical malaria cases (>60%) occur during a short period of 3-4 months,
 - the clinical attack rate of malaria is greater than 0.1 attack per transmission season in the target age group, and
 - AQ+SP remains efficacious (>90% efficacy).

SMC working group



Coordination Committee

Niger, Gambia, UNICEF, UCAD



SMC implementation
orientation meeting - Dakar

SECRETARIAT

WARN, MMV



Praia meeting to support
NMCP managers to develop
SMC implementation plans

CARN countries (Chad, Cameroon & and CAR) new members of the SMC working group

SMC in 2016



Funding

1. Red Cross*
2. Global Fund
3. UNITAID* (SMC Access)
4. World Bank
5. ALIMA
6. Save the Children
7. UNICEF*
8. MSF*
9. USAID/PMI*
10. MSH*

Technical Assistance

12. Speak Up Africa *
13. Cermes-Niger **
14. Centre Support Santé Internationale **
15. LSHTM **
16. MRTC **
17. University Gamal Abdel Nasser Guinea **
18. UCAD **
19. WHO Ghana & Morocco Pharmaco Vigilance centers**
20. WHO/TDR **
21. Malaria Consortium ***
22. WHO ***
23. CRS ***
24. MMV ****

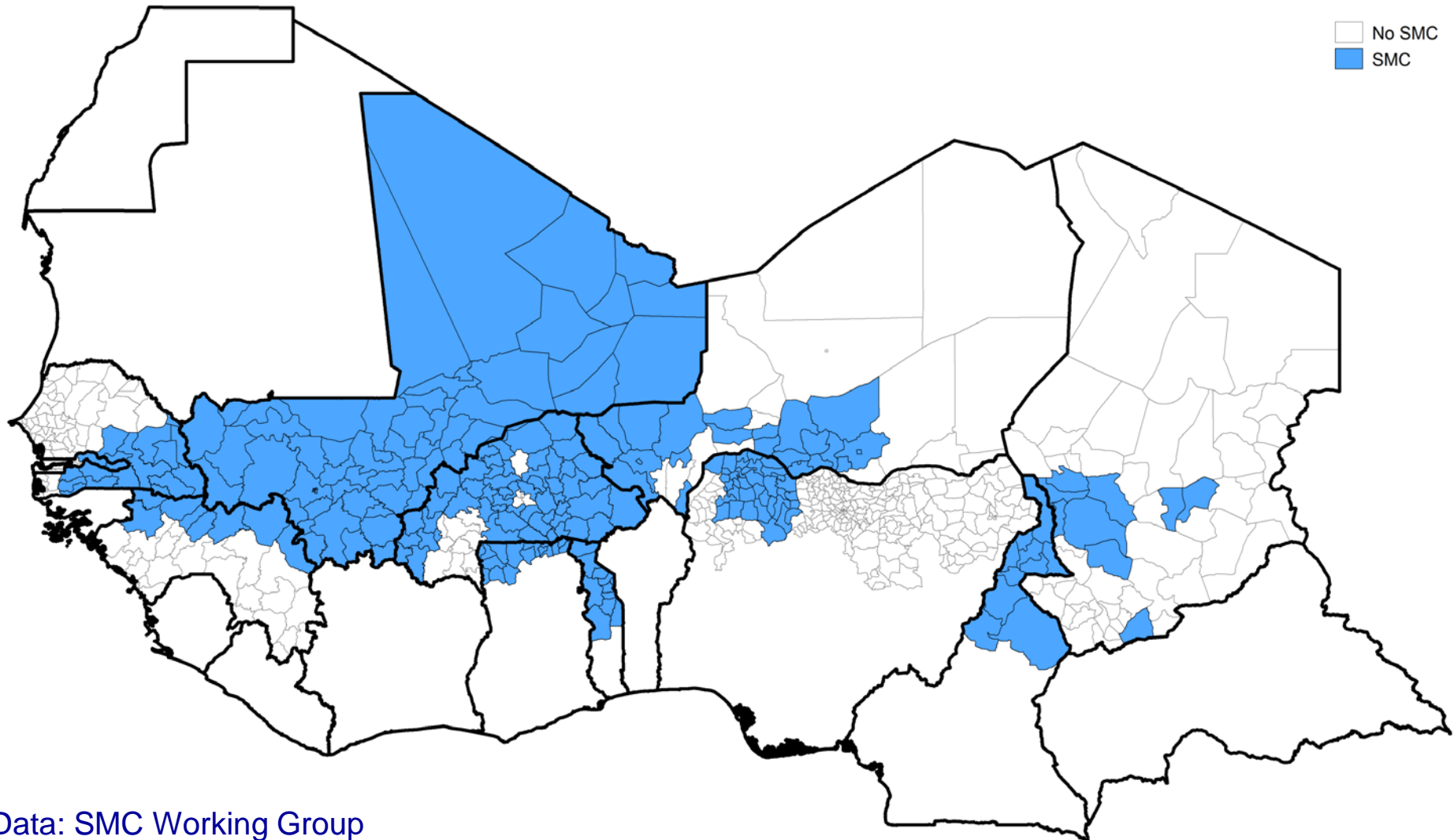
** Technical assistance also provided*

** BCC ** M&E *** Planning & Implementation **** Products access*

Progress of SMC implementation in 2016



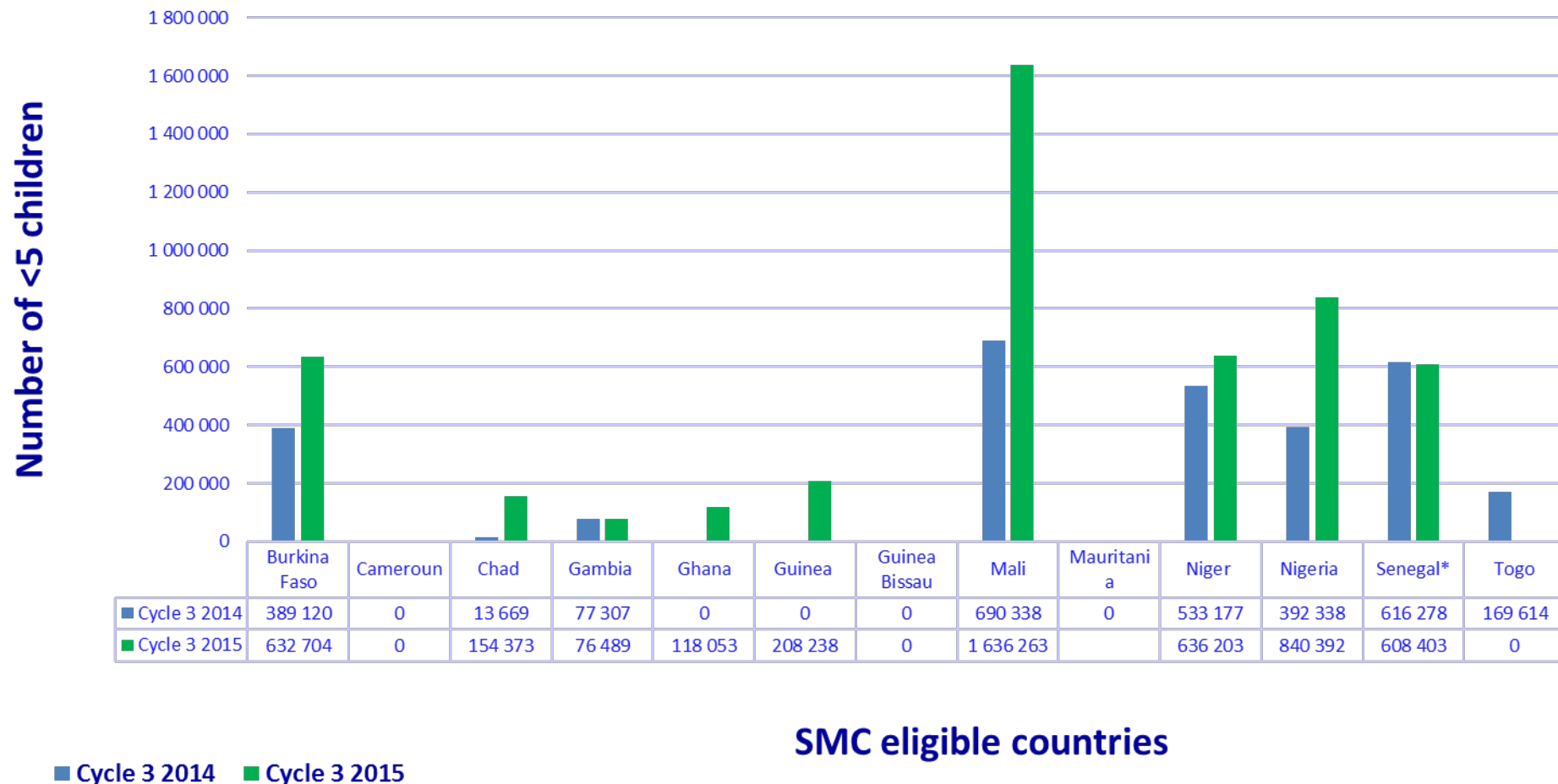
11 countries
15 million children protected



2014 vs 2015 SMC campaigns coverage



2014vs 2015 coverage for cycle 3



Challenges



Regional and global level

- WHO approved SP+AQ insufficient and expensive
- South-South cooperation to be strengthen
- Monitoring & Evaluation
- Set up one single coordination mechanism for SMC related activities at regional level

In-country level

- Preparedness (early planning and drugs ordering)
- Logistical issues
- More investments on M&E activities
- Strengthen domestic collaboration
- Strengthen coordination
- Weak pharmacovigilance systems
- Domestic fundraising

Conclusion



- Derives from IPTp & IPTi
- SMC recommended in 2012
- Targets 25 million children (15 m. already in 2016)
- Potential changing the malaria landscape
- Monitoring & Evaluation and more research needed
 - *Duration of SMC*
 - *Targeted intervention*
 - *Interventions integration*
 - *Extending age group to older siblings (e.g. in Senegal)*
 - *Long term impact on drug resistances*
 - *Alternatives to SPAQ*
 - *Etc...*